

The role of dermoscopy and digital dermoscopy follow-up in the clinical diagnosis of melanoma: clinical and dermoscopic features of 99 consecutive primary melanomas

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ABSTRACT **Background:** Early recognition is the most important intervention to improve melanoma prognosis. **Objective:** To report the value of dermoscopy and digital dermoscopy in the clinical diagnosis of malignant melanoma (MM). **Methods:** Retrospective analysis of 99 consecutive primary MMs diagnosed between 2010 and 2013. The MMs were divided into 3 groups: 1) the MM was the reason for consultation (MMC), 2) the MM was detected during routine control of nevi (MMRC), and 3) the MM was detected due to changes observed during digital dermoscopy follow-up (MMDFU). Clinical, dermoscopic and histologic features were assessed. **Results:** A total of 99 MMs were diagnosed in 89 patients (55% male) with a mean age of 50.8 (18-93) years. Of all the MMs, 35 were the reason for patient consultation (MMC), 52 were detected during routine control of nevi (MMRC) and 12 were diagnosed due to changes observed with digital dermoscopy (MMDFU). On clinical examination, 74.2 % of MMC met the 4 ABCD criteria, while only 30.7 % of MMRC and 8.3 % of MMDFU. Most MMC were correctly classified as malignant according to dermoscopy, but 44.2% of MMRC and only 16.7% of MMDFU. 22.9% of MMC, 50% of MMRC and 58.3% of MMDFU were in situ. Mean Breslow thickness was significantly lower in the MMDFU group (0.52 mm) than in the MMRC and MMDFU groups (0.77 and 1.43 mm respectively). **Conclusions:** The use of dermoscopy and digital dermoscopy allows the detection of MMs in early stages, even in the absence of specific criteria for malignancy.

Early recognition is the most effective intervention for improving the prognosis of patients with primary malignant melanoma (MM) [1]. Dermoscopy has shown to increase the sensitivity in the clinical diagnosis of melanoma from 60 to 90% with specificity as high as 95% [2]. However, melanoma may be clinically but also dermoscopically indistinguishable from melanocytic nevi making early recognition a diagnostic challenge [3], especially in incipient lesions. Furthermore, overlap of clinical features may lead to overlooking MMs and excising an excessive number of benign lesions [4]. Dermoscopic documentation of melanocytic lesions for the comparison of current and previous images in search of subtle changes over time, namely digital follow-up (DFU), has shown to be helpful in the diagnosis of early melanomas which might lack of specific criteria for malignancy. This approach has proved to be efficient in detecting early MMs without increasing the number of unnecessary excisions [5-7].

The use of baseline regional photographs, so-called total body photography (TBP), might facilitate the detection of new lesions, and visual changes in pre-existing lesions, by providing a comparative reference for subsequent examinations [8].

The combined use of TBP and digital dermoscopy, called the “two-step method” of digital follow-up [9], has been proposed an approach for the assessment of individuals at high risk, being potentially more accurate than the two strategies separately since it allow not only for the detection of MM with few dermoscopic criteria by comparison of dermoscopy records, but also for the detection of melanoma either presented as new lesions or arising from nevi that were not monitored by dermoscopy [10]. The inclusion of patients who are at high risk for melanoma in follow-up programs allows the detection of melanomas in early stages, with good prognosis, even in the absence of clinical and dermoscopic features of melanoma [11].

The aim of this study was to assess the clinical, dermoscopic and histologic features of melanomas diagnosed with the use of dermoscopy during routine skin examinations and the use of digital dermoscopy monitoring, compared with those melanomas that led to patient’s consultation.

Methods

We conducted a retrospective analysis of clinical and dermoscopic characteristics of 99 melanomas consecutively diagnosed over a 4-year period at the Dermatology Department of the Hospital Provincial del Centenario de Rosario, a third level hospital, and at the skin cancer department of a private diagnostic center. The study included primary lesions with clinical and dermoscopic pictures of acceptable quality to allow reliable evaluation. Patients who were referred with diagnosis of melanoma after excision or biopsy (incisional or

excisional) were excluded from the study as well as melanoma recurrences or cutaneous metastases of prior melanomas.

All melanomas diagnosed between January 2010 and December 2013 that met inclusion criteria for the study were collected from both databases. The MMs were divided into 3 groups: 1) the MM was the reason for consultation (Melanoma consultation, MMC), 2) the MM was detected during routine control of nevi using dermoscopy (Melanoma routine control, MMRC) and 3) the MM was detected due to changes observed during digital dermoscopy follow-up (Melanoma digital follow-up, MMDFU).

Clinical data such as age and gender of the patients and the localization and size of the lesions were incorporated along with the clinical and dermoscopic images in a Power-Point presentation (Microsoft Corp, Redmond, Washington). This collection was presented to two dermatologists with experience in dermoscopy (G.S. and C.A.) who performed both clinical and dermoscopic evaluation while blinded to the way of detection (MMC, MMRC or MMDFU), identity of the patients, and histologic features of the lesions.

For the clinical evaluation of the lesions, the ABCD clinical acronym for early detection of melanoma was used [11]. The dermoscopic evaluation was performed using the ABCD rule of dermoscopy proposed by Stolz, which is based on the evaluation of 4 criteria: asymmetry (A), abrupt borders (B), colors (C), and different dermoscopic structures (D) [13]. The total dermoscopy score (TDS) was calculated in each lesion, and they were classified as benign, suspicious or malignant.

As standard practice, patients who presented for nevi control undergo full clinical examination with a handheld dermatoscope (Dermlite DL100 and Dermlite II Pro Hybrid; 3Gen LLC, Dana Point, California). Those lesions with clear criteria for melanoma or those highly atypical are excised and sent for histopathology evaluation; suspicious lesions but with no criteria for melanoma alternatively can be scheduled for short-term follow-up. High-risk patients are included in a follow-up program with total-body photographs and digital dermoscopy, according to the 2-step method previously described [9], with follow-up visits once or twice a year. The latter evaluation aided with a digital dermoscopic device (Fotofinder dermatoscope, FotoFinder Systems GmbH, Germany). The criteria for inclusion in the follow-up program include moderate to severe atypical mole syndrome (AMS), presence of a congenital nevus of medium to giant size, AMS and previous melanoma, familial melanoma, presence of genetic mutations related to melanoma risk, and syndromes associated with melanoma risk.

Significant changes leading to excision of melanomas during digital dermoscopic monitoring were any of the following: symmetric enlargement, change in shape, focal changes in structure, regression, and changes in coloration. All new lesions observed during follow-up and exhibiting atypical

TABLE 1. Clinical characteristics according to ABCD acronym

Clinical criteria	Melanoma consultation (MMC) N=35	Melanoma routine control (MMRC) N=52	Melanoma digital follow-up (MMDFU) N=12	p*
Asymmetry	82.8%	61.5%	25%	<0.05
Irregular borders	80%	50%	16.6%	
Multiple colors	85.7%	57.6%	41.6%	
Diameter > 6mm	97.1%	71.1%	50%	
A+B+C+D	74.2%	32.6%	8.3%	

dermoscopic 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.

Each patient's written consent was obtained for all invasive procedures.

Statistical Analysis

The χ^2 test was used to compare qualitative variables, applying Fisher correction when needed because of the small sample size in tables of 2x2, and the t test was used to compare means. Differences were considered to be statistically significant at $P \leq .05$.

Results

Of the melanomas diagnosed between January 2010 and December 2013, 99 fulfilled the inclusion criteria of the study, 35 (35.3%) were the reason for patient consultation (MMC), 52 (52.5%) were detected during routine control of nevi using dermoscopy (MMRC), and 12 (12.2%) were detected due to changes observed during digital dermoscopy follow-up (MMDFU).

Population

The study population consisted of 40 female (45%) and 49 male (55%), with a mean age of 50.8 (18-93) years. The distribution according to gender was homogeneous among the three groups.

Clinical evaluation

Most of the MM that led to patient's consultation (MMC) were clinically asymmetric, had irregular borders and multiple colors, and had a diameter larger than 6 mm (Table 1). Of the MMRC, near 60% were asymmetric and had multiple colors, half had irregular borders, and more than 70% were 6 mm or larger. A quarter of the MMDFU were asymmetric, only 16.6% had irregular borders, about 40% had multiple colors and half of them were larger than 6 mm.

Almost 75% of the MMC fulfilled the 4 ABCD criteria, while a third of the MMRC and just 8% of the MMDFU (Figure 1). All differences were statistically significant.

Dermoscopic evaluation

Classification according to the ABCD rule of dermoscopy is shown in Table 2. Of MMC, 82.9% were correctly classified as malignant, 11.4% as suspicious and 5.7% as benign. In the MMRC group, 44.2% of MMRC were correctly classified as malignant, 46.2% as suspicious and 9.6% as benign. In the MMDFU group, only 33.3% were correctly classified as malignant, 16.7% as suspicious and 50% as benign.

Most of MMC (N=25, 71.4%) displayed multicomponent pattern according to pattern analysis, followed by reticular pattern in 7 (15%), 2 lesions had starburst pattern and 1 unspecific pattern. In the MMRC group, more than half had reticular pattern (n=28), while only 19 (36.5%) display multicomponent pattern. In this group, globular and unspecific pattern were seen in 2 and 3 cases respectively. Among the melanomas detected due to changes during digital follow-up (MMDFU), almost 60% (n=7) had reticular pattern and 25% (n=3) multicomponent pattern, 16.6% (n=2) showed globular pattern (Figure 2).

The most frequent morphological change was asymmetric enlargement in 6 out of 12 MMDFU, focal changes in structure were seen in 3 of 12 of the cases and regression in 1 of 12. One MM was excised because of symmetric enlargement and absence of other significant changes (Figure 3). One MM was excised because was noted as a new lesion in the comparative analysis of consecutive total body photographs.

Histology evaluation

The percentages of *in situ* melanoma among the groups were as follows: 22.9% in the MMC, 50% in the MMRC, and 58.3% in the MMDFU. 22.9% of the MMC were ulcerated, only 3.8% of the MMRC and none of the MMDFU. Of the invasive melanomas, the mean Breslow thickness was 1.43



Figure 1. (A-D) Clinical images of melanomas that led to patient's consultation (MMC), (E-H) melanomas detected during routine control (MMRC), and (I-L) melanomas detected due to changes during digital dermoscopy follow-up (MMDFU). (Copyright: ©2014 Salerni et al.)

TABLE 2. Dermoscopic characteristics

	Melanoma consultation (MMC) N=35	Melanoma routine control (MMRC) N=52	Melanoma digital follow-up (MMDFU) N=12	p*
Dermoscopy pattern				<0.05
Reticular atypical	15%	53.8%	58.3%	
Globular atypical	—	3.8%	16.7%	
Starburst	5.7%	—		
Unspecific	2.8%	5.7%		
Multicomponent	71.4%	36.5%	25%	
TDS	6.2	5	4.77	
Classification according to the TDS				<0.05
Benign	5.7%	9.6%	50%	
Suspicious	11.4%	46.2%	16.7%	
Malignant	82.9%	44.2%	33.3%	

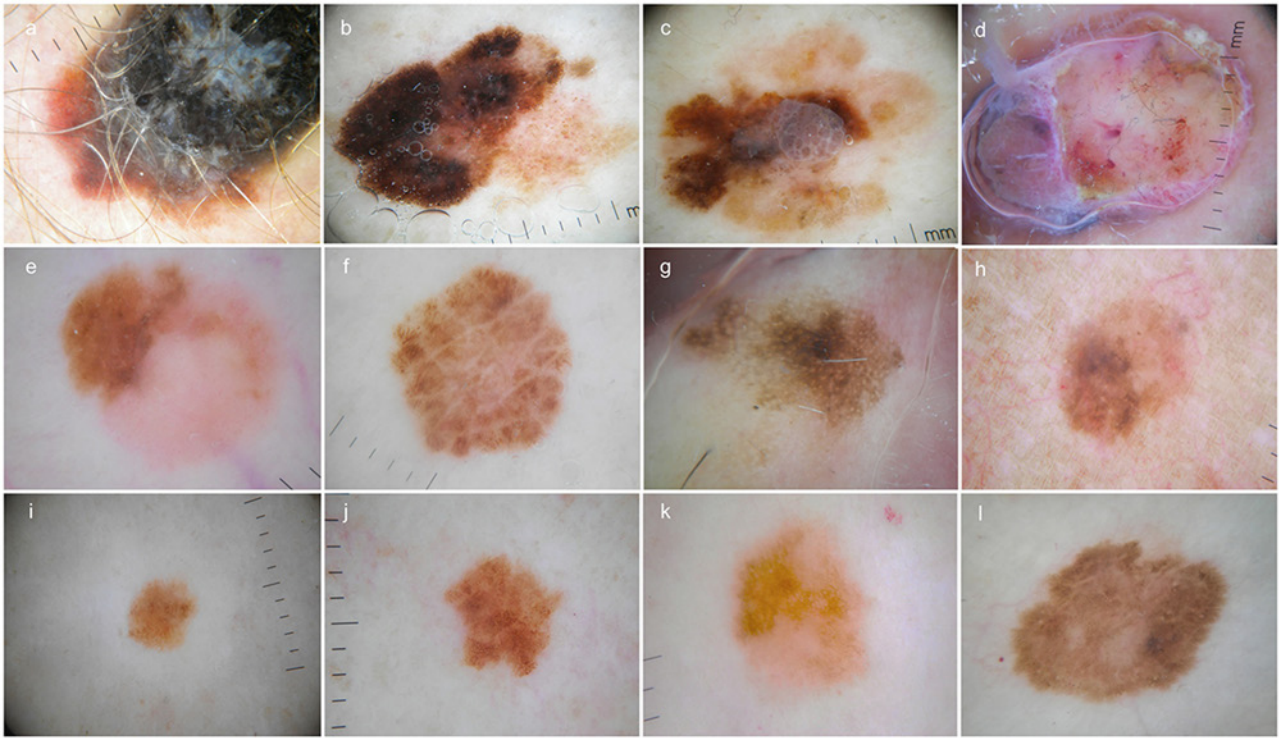


Figure 2. Dermoscopic images. MMC (A-D): (A) superficial extensive melanoma, Breslow 2.5 mm, Clark IV; (B) superficial extensive melanoma, Breslow 0.49 mm, Clark III; (C) superficial extensive melanoma, Breslow 1.7 mm, Clark IV; (D) Nodular melanoma, Breslow 3.7 mm, Clark V. MMRC (E-H): (E) superficial extensive melanoma, Breslow 0.75 mm, Clark III; (F) superficial extensive melanoma, Breslow 0.35 mm, Clark II; (G) In situ melanoma; (H) superficial extensive melanoma, Breslow 0.7 mm, Clark III. MMDFU (I-L): (I) in situ melanoma; (J) in situ melanoma; (K) superficial extensive melanoma, Breslow 0.7 mm, Clark III; (L) superficial extensive melanoma, Breslow 0.6 mm, Clark III. (Copyright: ©2014 Salerni et al.)

mm in the MMC group, 0.77 mm in the MMRC and 0.52 mm in the MMDFU. All these differences were statistically significant (Table 3).

Clinical stage at diagnosis

The clinical stage of the melanomas was classified according to the American Joint Committee on Cancer staging system [14]. Of the MMC, 8 (22.8%) presented as stage 0 at diagnosis and 14 (40%) as stage IA, 5 (14.2%) presented as stage IB, 6 (17.1%) as stage II and 2 (5.7%) as stage III, none of the MMC presented as stage IV. In the MMRC group, 26 (50%) presented as stage 0, 21 (40.3%) as stage IA, 3 (5.7%) as stage IB and 2 (3.8%) as stage II; none of the MMRC presented as stage III or IV. Among the MMDFU, 7 (58.3%) presented as stage 0 and 5 (41.7%) as stage IA, none presented as stage IB, II, III or IV. Differences among the different groups were statistically significant.

Of the MMC, 13 (37.1%) required sentinel node biopsy, while only 5 among the 52 MMRC (9.4%) and none of the MMDFU.

Discussion

Early recognition is the most effective intervention to improve melanoma prognosis [1]. Over the past decades, efforts in

secondary prevention have contributed to the stabilization of melanoma mortality.

The ABCD acronym was designed almost 30 years ago to provide the general public and primary care professionals a memorable and useful tool to aid in the early recognition of melanoma [12]. The parameters asymmetry, border irregularity, color (multiple colors), and diameter larger than 6 mm are used globally in medical education and in the lay press to provide simple parameters for evaluation of pigmented skin lesions which may require a more comprehensive examination by a specialist. While the A, B, and C criteria have been widely accepted, the emergence of reports with a significant proportion of melanomas with a diameter < 6 mm [15,16], has generated controversy around the criterion D, questioning its usefulness in recognizing incipient lesions. In our study, the vast majority of the melanomas that led to patient's consultation (MMC) fulfilled the 4 ABCD criteria with a 97% of lesions with a diameter > 6 mm. More than 70% of the MMRC had a diameter > 6 mm; one third of these melanomas fulfilled the 4 ABCD criteria simultaneously. In the MMDFU group, melanomas most melanomas were symmetric and did not have irregular borders, only 40% had multiple colors and only half had a diameter > 6 mm. Less than 10% of the MMDFU fulfilled the 4 ABCD criteria simultaneously.

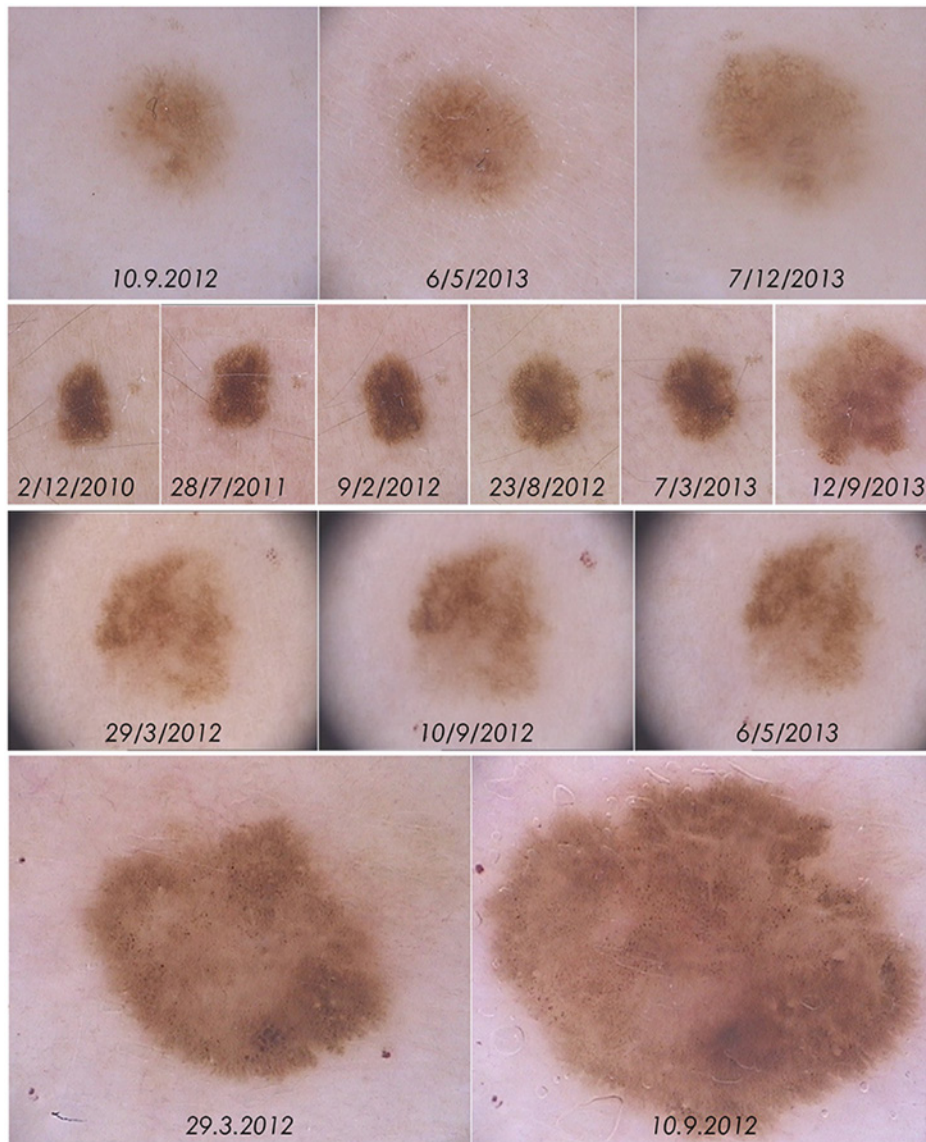


Figure 3. Melanomas detected during digital dermoscopy follow-up (MMDFU) and changes that led to excision. Changes correspond to the lesions I (first row), J (second row), K (third row) and L (fourth row) in Figure 2. (Copyright: ©2014 Salerni et al.)

TABLE 3. Histologic characteristics

	Melanoma consultation (MMC) N=35	Melanoma routine control (MMRC) N=52	Melanoma digital follow-up (MMDFU) N=12	p*
In situ melanoma	22.9%	50%	58.3%	<0.05
Invasive melanoma	77.1%	50%	41.7%	
Ulceration	22.9%	3.8%	0%	
Breslow (mean)	1.43 mm	0.77 mm	0.52 mm	

In 2004, the ABCD acronym was revised, the addition of E, for evolution, has substantially improved the ability of clinicians and the general population to detect melanomas at an early stage by recognizing their natural dynamics. The latter criterion is especially important for the diagnosis of nodular melanoma, which frequently, at least initially, is symmetrical, with regular borders and few colors [17].

Dermoscopy has been shown to improve the diagnostic accuracy for early melanoma detection [18-20], and currently training and utilization of dermoscopy is recommended for clinicians routinely examining pigmented skin lesions [21]. Most melanomas that led to patient's consultation were already clinically suspicious (3/4 fulfilled the 4 ABCD criteria) and more than 80% were correctly classified as malignant according to ABCD rule of dermoscopy, with less than 6% misclassified as benign. In the MMRC group, near 40% of the melanomas were correctly classified as malignant, with a significant proportion of melanomas misclassified and benign or suspicious (almost 10% and 50% respectively). These findings support the recommendation that dermoscopy should be used for all lesions, and not just for those suspicious from the clinical point of view [22], since melanomas detected in this group corresponded to lesions that the patient was unaware of at the time of consultation or lesions that didn't caught patient's attention previously. In a recent study, Salerni et al [11] compared melanomas detected in a follow-up program with melanomas referred to a melanoma unit, they found 36% of melanomas detected during surveillance of patients at risk for melanoma misclassified as benign according to the ABCD rule of dermoscopy with a significantly lower mean TDS than the referred melanomas. They conclude that the surveillance of patients who are at high-risk for melanoma aided by dermoscopy allows the detection of melanomas low index of suspicion according to dermoscopy.

It has been reported that melanoma may simulate benign melanocytic nevi even under dermoscopy examination [3]. On the basis that benign lesions remain stable whereas melanoma tend to change over time, digital follow-up of melanocytic lesions has been proposed as a strategy to recognize melanomas that may lack distinct dermoscopic features at baseline [23]. In our study, 11 of the 12 MMDFU were detected only due to changes observed during digital follow-up. In this group, only one third of the melanomas were correctly classified as malignant according to the ABCD rule of dermoscopy, with a mean TDS of 4.77 (significantly lower than the MMC and MMRC group), pointing out that digital follow-up allow for the detection of early melanoma, when specific structures or criteria for malignancy may not be present yet. Similarly, in the ten-year experience in the surveillance of high-risk melanoma patients in a melanoma unit [10,24], 98 melanomas were diagnosed, with less than half correctly classified as malignant according to dermoscopy algorithm.

Breslow thickness of the primary tumor is the dominant prognostic factor in melanoma. Criscione and Weinstock [25], analyzed data from the Surveillance Epidemiology and End Result (SEER) program of the National Cancer Institute, they found that the most substantial change across the past decades occurred in the proportion of melanoma *in situ*, which rose from 25% in 1988 to 38% in 2006. In our study, proportion of melanoma *in situ* varies according to the observed group: less than one quarter among the melanomas that led to patient's consultation, but rising to 50% almost 60% with the use of dermoscopy and digital dermoscopy respectively; highlighting the benefits of the latter approaches in the recognition of melanoma at early stages.

Regarding this issue, a meta-analysis was recently conducted to assess the evidence of follow-up of melanocytic skin lesions with digital dermoscopy in the management of individuals at risk for melanoma [26]. This analysis provided evidence that digital dermoscopy follow-up of melanocytic skin lesions with digital dermoscopy demonstrated the early detection of melanomas with a low rate of excisions. With the use of this diagnostic strategy, the proportion of *in situ* melanoma and thin melanomas were higher than expected in general population. Almost 60% melanomas of the melanomas detected due to changes during digital follow-up were *in situ*; they were thinner among invasive ones than the MMC and MMRC; and none were ulcerated. None of the MMDFU and less than 10% of the MMRC required sentinel lymph node biopsy (SNLB), while almost 40% of the MMC have indication for SLNB, with a 6% of the patients in this group classified as stage III at the time of diagnosis.

In this study we report the value of dermoscopy examination and digital follow-up in the clinical diagnosis of melanoma in a series of consecutive melanomas. Our findings confirm prior observations that the clinical ABCD acronym might only allow for the detection of evolved melanomas, since most melanomas that led to patient's consultation were already invasive. In this setting, the current efforts in public and medical education might have no substantial effect. The routinely use of dermoscopy in diary practice allow for the detection of melanomas with low index of suspicion of which the patients are unaware. In the context of high-risk patients, the use of digital follow-up enables the detection of incipient melanomas that lack not only clinic but also dermoscopic criteria for malignancy.

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