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# The importance of total-body photography and sequential digital dermatoscopy for monitoring patients at increased melanoma risk

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## Summary

**Background and objectives**: The incidence of melanoma is rising and prevention plays an important role. Multiple nevi as well as a medical history of melanoma are important risk factors. In affected patients, a two-step algorithm consisting of total-body photography (TBP) and sequential digital dermatoscopy (SDD) is a helpful diagnostic tool.

**Patients and methods**: This was a retrospective observational study that lasted six years in order to evaluate the significance of the two-step algorithm. Cases were evaluated based on distinct dermoscopic patterns and statistical analyses were performed with the latest version of SPSS.

**Results**: 6020 dermoscopic images of 214 patients were included. TBP was performed at a mean interval of 16.9 months (SD ± 1.43 months), while SDD was performed every 9.9 months (SD ± 1.68 months). The number needed to excise was 4.6 and the number needed to monitor was 548. Excisions were mostly performed because dynamic changes were observed. A total of eleven melanomas were detected and had a mean tumor thickness of 0.44 mm (SD ± 0.15 mm; range 0.2–0.6 mm).

**Conclusions**: Invasive melanomas had a tumor thickness of less than 0.6 mm, thus providing evidence of an effective strategy for early melanoma detection. Excisions of benign nevi were minimized as indicated by a low number needed to excise.

## Introduction

According to available data, melanoma is the seventh most frequent malignancy with an estimated incidence of 100,300 cases in Europe in 2012. Both the incidence of melanoma and its five-year survival rate have increased during the last decade in several countries. This is mostly due to improved early detection of melanomas, which has resulted in a lower tumor thickness of primary melanomas [1, 2]. Apart from genetic factors, a large number of common and atypical nevi are the most relevant risk factors for developing a melanoma. In particular, having more than 100 common nevi results in a sevenfold higher risk than having less than 15 common nevi, and individuals with five atypical nevi have a risk of developing malignant melanoma that is about six times that of individuals with no atypical nevi. It is therefore advisable to perform risk-adapted screenings for these patients [3–5].

Dermatoscopy has improved early recognition of melanoma dramatically. Using distinct algorithms (e.g. ABCDE rule, 3 C's, 7-point checklist, pattern analysis), this technique enables diagnosis of melanoma at a very early stage [6]. The two-step algorithm of digital follow-up (DFU) consisting of total-body photography (TBP) and sequential digital dermatoscopy (SDD) is a valuable tool for recognizing changes in already documented lesions as well as for detecting new lesions [7–9]. The FotoFinder® system is a device used in preventive dermato-oncology that provides a total-body photography module and a dermatoscopy module in order to follow-up

 

lesions with a two-step algorithm. Patients with multiple nevi benefit from this method, especially patients with multiple atypical nevi. This is because subtle changes within a lesion can be detected, resulting in an improved sensitivity of melanoma detection [8]. Furthermore, digital follow-up reduces the number of unnecessary excisions of benign lesions [9]. The current literature does not appear to provide distinct recommendations on the lengths of DFU intervals; however, it is suggested that short-term follow-ups (every three months) be reserved for single suspicious lesions, while middle- and long-term follow-ups (6- to 12-monthly) should be performed for monitoring multiple lesions in patients with numerous nevi [8–14].

The aim of this study was to evaluate the usefulness of the two-step algorithm in early melanoma detection in a cohort of high-risk patients.

## Methods

We performed a retrospective observational study in order to evaluate the significance of TBP and SDD using the FotoFinder® system at the Department of Dermatology and Venereology in Graz. All clinical investigations were conducted according to the principles of the Declaration of Helsinki. Patients gave their consent prior to enrollment, and we obtained approval of the local ethics committee (Approval number 27–421 ex 14/15). All patients who underwent preventive examinations with this device between November 2011 until January 2015 were included. At least two documented examinations were required for inclusion.

Clinical and dermoscopic images were obtained using the FotoFinder bodystudio® ATBM (automatic total-body mapping). This procedure was performed in two steps: first, standardized clinical images of the entire body surface were taken with a software-controlled reflex camera. Overall, 20 images per patient were saved during one examination. The clinical images were then supplemented with dermoscopic images using the FotoFinder medicam-800HD. TBP was performed every two sessions and SDD was carried out at every session.

In addition, the following parameters were collected for each patient: *(i)* sex, *(ii)* age, *(iii)* total number of nevi, *(iv)* presence of atypical mole syndrome, *(v)* history of malignant melanoma, *(vi)* number of examinations and average time interval for both TBP and SDD. In case of any excisions, the above-mentioned data were supplemented with the histopathological report and the reason for excision (dermoscopic changes during DFU versus development of a new lesion). Two experts (RHW and RFP) performed dermatoscopic evaluations of the images. The dermatoscopic criteria that were applied are based on a proposal by Hofmann-Wellenhof et al. [10] and were slightly modified for our study (omission of the non-classified type; unifying the terms "eccentric hyperpigmentation" and "eccentric hypopigmentation" to the term "eccentric", adding the term "homogeneous"). The global dermoscopic pattern was rated as reticular, globular, homogeneous, globular-homogeneous, reticular-globular or reticular-homogeneous. The global type of pigmentation was rated as homogeneous, central hyperpigmented, central hypopigmented, patchy or eccentric.

Multivariate statistical analyses were performed using data frequency comparisons with the Chi-square test as well as the Pearson and Spearman correlations with the use of the latest SPSS software (IBM SPSS Statistic 25).

## Results

### Patient characteristics and follow-up intervals

Data of 361 patients were screened. 147 patients were excluded due to either missing follow-up data or low image quality. A total of 6020 dermoscopic images from 214 patients (122 men; 57 %) were included. The mean age of patients was 43.8 years (standard deviation [SD] ± 11.8 years, range: 13–78 years). The mean age of female patients was 42.8 years (SD ± 9.7 years), and the mean age of male patients was 44.6 years (SD ± 13.2 years). Overall, 74 patients (34.6 %) were diagnosed with an atypical mole syndrome. Of these, 28 (37.8 %) had a positive history of previous melanoma. The total number of nevi per patient is shown in Table 1.

An average of 214 patients had 2.4 visits, with total-body photography ranging from one to eleven examinations. Dermatoscopic imaging resulted in a mean of 4.3 images per patient and was taken at every visit (range: 1 to 21 images). TBP was performed at a mean interval of 16.9 months (SD ± 1.43 months). The mean number of TBP sessions per patient was 2.4. The SDD images were taken at a mean interval of 9.9 months (SD ± 1.68 months) with a mean of 4.3 sessions per patient. The dermatoscopic patterns observed and the different types of pigmentation are shown in Table 2.

**Table 1** Number of nevi per patient.

| Total number of nevi | All patients (n = 214) | Men (n = 122) | Women (n = 92) |
|---|---|---|---|
| < 20 | 0 | 0 | 0 |
| 20–50 | 1 | 1 | 0 |
| 50–100 | 7 | 1 | 6 |
| 100–150 | 16 | 10 | 6 |
| 150–200 | 34 | 13 | 21 |
| > 200 | 156 | 97 | 59 |


 

**Table 2** Frequency of dermoscopic pattern and different types of pigmentation.

| | All lesions (n = 6020) | Men (n = 122) | Women (n = 92) |
|---|---|---|---|
| *Dermoscopic pattern* | | | |
| Reticular | 544 | 308 | 236 |
| Globular | 508 | 248 | 260 |
| Homogenous | 1070 | 545 | 525 |
| Homogenous-globular | 1222 | 662 | 560 |
| Reticular-globular | 876 | 459 | 417 |
| Reticular-homogenous | 1800 | 1078 | 772 |
| *Pigmentation* | | | |
| Uniform in color | 1433 | 697 | 736 |
| Centrally hyperpigmented | 1199 | 702 | 497 |
| Centrally hypopigmented | 389 | 239 | 150 |
| Multifocal hypo- and hyperpigmentation | 2353 | 1295 | 1058 |
| Eccentric | 646 | 367 | 279 |

## Characteristics of lesions and results of histopathology

A total of 51 suspicious lesions including eleven melanomas were excised from 33 patients during the study period. The histopathological diagnoses are summarized in Table 3. The number needed to excise (NNE) amounted to 4.6. In other words, 4.6 excisions had to be done to diagnose one melanoma. Moreover, a total of elven melanomas detected among 6020 documented lesions had a number needed to monitor (NNM) of 548. Excisions were mostly performed because abnormalities were seen with SDD (35/51; 68.6 %). Nine out of these 35 lesions showing dynamic changes were diagnosed as melanoma.

The eleven detected melanomas were diagnosed in seven patients (2 women and 5 men). The average age in this group was 58.6 years (range 44.7 to 73.6 years). Seven melanomas were located on the trunk and four melanomas were detected on the extremities. All melanomas diagnosed in women (n = 3) were found on the trunk, while melanomas diagnosed in men (n = 8) were located on the trunk (n = 4) and extremities (n = 4). We diagnosed one melanoma *in situ* and ten invasive melanomas with a tumor thickness according to Breslow between 0.2 mm and 0.6 mm. The mean tumor thickness of the invasive melanomas was 0.44 mm (n = 10; SD ± 0.15 mm).

**Table 3** Frequency of histopathological subtypes of excised lesions.

| Histopathological subtype | Number (n = 51) |
|---|---|
| *Malignant melanoma* | *11 (21.6 %)* |
| Melanoma in situ (MIS) | 1 |
| T1a-melanoma | 9 |
| T1b-melanoma | 1 |
| *Nevi* | *37 (72.5 %)* |
| Common nevi | 10 |
| Congenital nevi | 1 |
| Atypical nevi | 26 |
| *Other lesions* | *3 (5.9 %)* |
| Cystically dilated hair follicle with inflammatory infiltration | 1 |
| Scar tissue with inflammatory infiltration | 1 |
| Collision-tumor: Junctional nevus + angioma + lymphangioma | 1 |

## Statistical correlations

There was a significant negative correlation between the presence of a globular or homogeneous-globular pattern and increasing age ($p < 0.001$ and $p < 0.05$, respectively). However, the reticular-homogeneous pattern was significantly associated with an increased age ($p < 0.05$). Concerning types of pigmentation the following significant correlations were observed:

- Negative correlation between increasing age and centrally hyperpigmented lesions ($p < 0.01$),
- Association of multifocal hypo- and hyperpigmented lesions with increasing age ($p < 0.001$).

Due to the small number of melanomas, associations between the detection of melanomas and the demographic parameters of the study population were not statistically significant.

# Discussion

The aim of this retrospective study was to evaluate the significance of the two-step algorithm in terms of early recognition of melanoma in 6020 images over a period of six years. Several strategies have been suggested for high-risk patients regarding early detection of melanoma such as self-examination, total cutaneous examination, dermatoscopy and TBP. There is growing evidence that total-body photography and

 

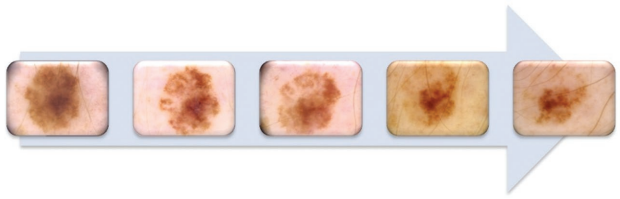

**Figure 1** Regressive nevus during a period of four years.

digital follow-up are useful tools for surveillance in high-risk populations in order to minimize excisions of benign lesions without overlooking melanoma [7–13].

All excisions were performed either due to alterations of already recorded lesions (68.6 %) or high-grade atypia of newly documented lesions (29.4 %); the remaining 2 % were atypical nevi without a statement concerning the reason for excision (Figures 1, 2). These results are in line with previous reports that documented a similar distribution of "reasons for excision" when applying the two-step algorithm. The ratio between excised melanomas and benign lesions resulted in an NNE of 4.6. In the context of the current literature, our NNE was smaller than the overall NNE of 8.7 that was reported for a multicenter study covering a ten-year interval. Of note, the latter was carried out at several clinics (including specialized and non-specialized centers) and may therefore not be eligible for a head-to-head comparison with our results. It is also well known that DFU is a technique that requires training, experience and specific equipment; this might explain the higher NNE in the study performed by Argenziano et al. This group also mentioned that the accuracy of melanoma detection was improved in a subanalysis limited to the group of specialized centers [11, 12], [14–16]. Keeping the NNE low is important, as unnecessary excisions of lesions are associated with increased morbidity and costs for the health care system. DFU makes recognition of melanoma easier at an earlier stage, and is therefore an ideal method to minimize excisions of benign lesions in high-risk patients [17–19]. These results also indicate that TBP and SDD should only be performed by clinicians experienced in dermatoscopy and in special clinical settings.

Our results show a number needed to monitor of 548, although the meta-analysis of Salerni et al. showed a lower NNM of 348 [17]. However, our results are still well within the reported range of NNMs in the included studies (range 31–1008) [17]. The meta-analysis by Salerni et al. showed that the studies with the lowest reported NNMs corresponded to the studies with the smallest number of lesions monitored per patient (range between 1.3 and 1.5 lesions monitored per patient). Of note, two of the aforementioned studies only focused on short-term follow-up and did not consider the patients' risk. Obviously, it is not unexpected that focusing on the assessment of single suspicious lesions results in a low NNM, as the lesions selected for short-term follow-up can usually be divided into two categories: on the one hand atypical nevi without any changes (left unexcised), and on the other hand atypical lesions with dynamic changes that require excision due to the increased possibility of being a melanoma [17].

In our study, a total of elven melanomas were detected with the two-step algorithm. One of these was an *in situ*

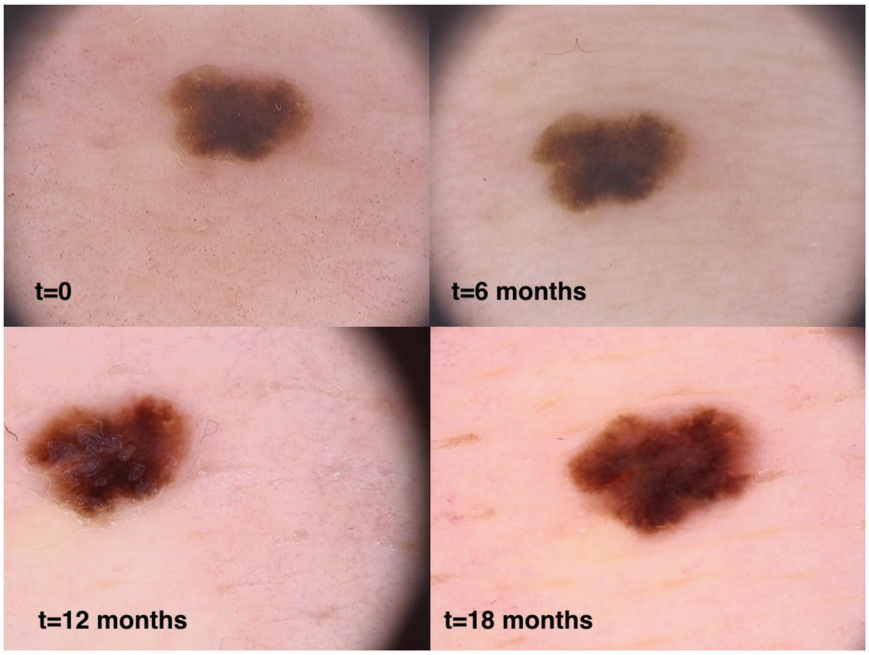


**Figure 2** Malignant melanoma (tumor thickness 0.5 mm). The timeline shows the changes over a period of 18 months.


 

melanoma and ten were invasive melanomas with a mean tumor thickness of 0.44 mm. Our results are similar to those of Salerni et al. [14], who observed a mean tumor thickness of 0.53 mm using the two-step algorithm. These results suggest that this method is a valuable way to detect melanomas at an early stage. It seems reasonable to assume that at least some patients monitored by the two-step algorithm may have a better prognosis in terms of 5- and 10-year survival rates. However, it is worth noting that in a retrospective study investigating the value of monitoring patients with multiple nevi, about one third of diagnosed melanomas were not detected previously by TBP [18–20].

The average time interval in our study was 16.9 months for TBP and 9.9 months for SDD. The difference in intervals between TBP and SDD imaging is due to the fact that SDD images were recorded in every session, while TBP was performed every two sessions. However, there are no precise recommendations concerning the length of intervals between two examinations with DFU. A review of the current literature suggests intervals of approximately three months (short-term-DFU) for assessment of single, suspicious melanocytic lesion without any dermatoscopic features of melanoma. In contrast, medium- and long-term DFU (6- to 12-monthly schedule) should be used to monitor multiple lesions in patients with numerous nevi with or without a personal and/or familial history of melanoma [17]. Consequently, high-risk patients need to undergo regular DFU, and 6- to 12-month intervals for DFU should be chosen for patients with atypical mole syndrome. In a prospective study with 688 patients carried out by Haenssle et al., the authors suggest an individualized follow-up with digital dermatoscopy depending on the individual patient's risk. Patients with known FAMMM syndrome (familial atypical mole and multiple melanoma syndrome) need to undergo short-term follow-ups of three months. However, for patients with atypical mole syndrome, a follow-up every 6 to 12 months seems to be adequate. Patients with multiple common nevi and no additional risk factors did not benefit from digital dermatoscopy. Similar recommendations were proposed by Blum et al. in 2014 based on the current skin cancer screening intervals in Germany. The authors also suggested risk-adapted skin cancer screening with follow-up intervals similar to those proposed by Haenssle et al. Several studies provided evidence for "slow-growing" melanomas, which can only be detected by performing long-term follow-ups as they may initially lack specific criteria for malignancy, either clinical or dermoscopic [11, 17–22].

To summarize, our study provided evidence for the effectiveness of the two-step algorithm (TBP and SDD) in high-risk patients, in terms of early recognition of melanomas while minimizing excisions of benign lesions. Therefore, it seems reasonable to perform sequential digital follow-ups in high-risk patients with a combination of TBP and SDD. However, intervals between examinations may differ depending on short-term follow-up versus long-term follow-up and the individual risk of melanoma for the patient.

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