


**New Diagnostic Method for Lesions With Transpidermal Melanocytic Migration**

Transepidermal melanocytic migration (TEM) is a histological feature that is frequently observed in malignant melanoma but may also occur in nevi (eg, Spitz nevi, acral nevi). Pagetoid TEM is considered a key indicator of malignant disease. We refer to an unusual case report by Kerl et al. in a young female patient. Eleven melanomas were originally diagnosed within 10 years, and in a comprehensive retrospective diagnosis, these could be reclassified as nevi. (See Kerl et al. for details of the patient’s medical history and the context of this case.) Herein, we report on the application of a new diagnostic method for melanocytic lesions to the issue of TEM as melanoma indicator.

**Methods**

Recently, a new diagnostic method has been described for malignant melanocytic melanoma, which is based on the stepwise 2-photon excited melanin fluorescence (STPMF) of melanosomes. The mechanism of STPMF is illustrated in Figure 1; for a description of the method used see Eichhorn et al. This fluorescence shows a high information content. The STPMF spectra of the fluorescence from melanocytes (Figure 2A), from nevus cell nevus (Figure 2B), and from malignant melanocytic melanoma (Figure 2C) are characteristically different and diagnostically useful. The mechanism of STPMF is illustrated in Figure 1C; for a description of the method used (briefly, to measure melanin fluorescence in the skin, separated from the other fluorophores) see Eichhorn et al. Furthermore, nonaltered dermis is characterized by a specific signal from collagen, which occurs at the 400-nm second harmonic of the excitation radiation. With this collagen signal, both nevus components in the dermis (eg, the compound nevus) and melanoma invasion through the basal membrane can be characterized. This finding applies to the tissue in vivo and ex vivo and in histological preparations. The parents of the patients were informed about the study and provided written informed consent to a molecular workup of all tissues and to the publication of the case report. Institutional review board approval was not necessary in this setting.

In this study, 8 histological preparations of specimens from the patient described by Kerl et al. were examined with STPMF. According to the original diagnosis, the samples included 1 melanoma in situ, 2 melanomas in situ in conjunction with a compound nevus, 3 atypical compound nevi, and 1 compound nevus. For the STPMF measurement of fluorescence, the preparations were each covered with a measuring grid with 50-μm increments. In this way, the entire epidermis and the dermis, to a depth of up to 900 μm, were detected. The result per sample—depending on its size—was 250 to 1000 fluorescence spectra, each associated with a tissue region of about 30 μm in diameter.

**Results**

No signs of melanocytic malignant degeneration were found in any of the 8 samples, including those from the lesions originally classified as melanoma in situ. The fluorescence spectra indicate uniformly benign compound nevi. These results correspond to the revised diagnostic findings of these samples described in the article by Kerl et al.

It should be noted that the histological observation of TEM in the 8 samples is equivalent to detection of the occurrence of fluorescence of melanosomes in the upper layers of the epidermis using the method described herein. But, interestingly, the spectral properties of these melanosomes correspond to those from nevus cells, not to those from melanocytes (Figure 2). This finding agrees with the fact that the absence of melanosome transfer to the keratinocytes is characteristic of nevus cells. However, the latter usually form nests, which are missing in this case.

It is worth mentioning that in the case of TEM in histologically proven malignant melanomas, the fluorescence of the ascending cells corresponds to that of melanoma cells.

**Figure 1. Schematic Representation of Different Types of Fluorescence Excitation of Organic Fluorophores (Simplified)**

The figure shows a Jablonski diagram. The length of the arrow indicates the energy of the photon (wavelength is written next to the arrow). The solid arrows indicate laser photons, and the dashed arrows indicate fluorescence photons. A. Conventional 1-photon excitation; B, simultaneous 2-photon excitation; C, stepwise 2-photon excitation of melanin fluorescence. A and B illustrate excitation suitable for measuring the conventional autofluorescence of skin tissue. The corresponding fluorophores show no absorption of 800-nm photons; therefore, the latter can be used for fluorescence excitation only in a simultaneous 2-photon absorption process. However, melanin has sufficient absorption at 800 nm and therefore can absorb 2 such photons in a stepwise absorption process (mechanism illustrated in panel C), which is substantially more effective than the mechanism shown in panel B. This way, the ultraweak fluorescence of melanin in skin, which otherwise is completely masked by the autofluorescence, is detectable. (For details, see Eichhorn et al.)
Discussion | The results show that STPMF-based diagnosis in the histologically complex case of TEM gives clear results. This new method shows an early malignant melanocytic degeneration.
with high sensitivity, even before it is histologically detectable; therefore, the complete absence of such melanoma spectra among the total of 5650 measured tissue areas of the 8 samples is a sure indication of their uniform benignity.

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Lesion Selection by Melanoma High-Risk Consumers During Skin Self-examination Using Mobile Teledermoscopy

Mobile teledermatoscopy (MDT) for the early detection of skin cancer uses smartphones with dermoscope attachments to magnify, capture, and transfer images remotely. Using the asymmetry–color variation (AC) rule, consumers achieve dermoscopy sensitivity of 92.9% to 94.0% and specificity of 62.0% to 64.2% for melanoma.

This pilot randomized trial assessed lesions of concern selected by consumers at high risk of melanoma using MDT plus the AC rule (intervention, n = 10) or the AC rule alone (control, n = 12) during skin self-examination (SSE). Also measured were lesion location patterns, lesions overlooked by participants, provisional clinical diagnoses, likelihood of malignant tumor, and participant pressure to excise lesions.

Methods | Ethics approval, informed consent, and intervention group (n = 10) characteristics were described previously.1 All participants were provided with an AC rule fact sheet and standardized SSE instructions. Participants underwent clinical skin examinations (CSEs) 3 to 6 months after SSEs to assess lesions of concern found during SSE and additional lesions potentially overlooked.

Results | Participants’ characteristics were similar in the intervention and control groups: overall, 60% male; working full time, 68%; personal history of melanoma, 73%; and body areas with moles, 59%. During SSE, 107 lesions were identified (66 in the intervention group and 41 in the control group; Figure, A), with patterns of body lesion locations similar for both groups. Figure, B and C, compares lesions identified during SSE and provisional clinical diagnosis during CSE. Likelihood of malignant tumor and pressure by participants to excise lesions during CSE are listed in the Table. Forty-two additional lesions not pointed out by participants were noted during CSE (20 in the intervention group and 22 in the control group), including 1 clinically presenting as melanoma (dysplastic nevus), 2 basal cell carcinomas (1 confirmed in the intervention group and 1 resolved before surgery in the control group), and 1 squamous cell carcinoma (confirmed in the intervention group) (Table). On average, participants’ SSE in both groups missed 2 lesions (intervention median [SD], 2 [1.43]; control median [SD], 2.09 [0.93]).

Discussion | Consumer-selected lesions were unlikely to be malignant, although more than one-third were dysplastic nevi. During CSE, the dermatologist detected other higher-priority skin lesions. These lesions were in hard-to-see body areas and might have been missed during SSE.

Participants in both groups selected lesion locations that reflect the SSE primary body areas (arms, face, and front of legs) reported by Mujumdar et al.2 Both groups also selected lesions on the back, shoulders, and legs, reflecting findings by Carli et al.4 Our participants did not select lesions in sexually sensitive5 or harder-to-see areas.

Previously, Boone et al3 found a lower proportion of missed lesions in partner-assisted compared with unassisted SSEs. We instructed participants to select 3 to 5 lesions during SSE, which may have contributed to participants missing lesions and explain some discrepancies between participant and dermatologist assessment.

Future studies need to instruct participants to also submit location photographs of lesions to aid re-identification during CSE. Consumers with many moles, such as participants in