In Vivo Epiluminescence Microscopy: Improvement of Early Diagnosis of Melanoma

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The majority of pigmented skin lesions can be diagnosed correctly on the basis of clinical criteria; however, there remain a surprisingly high number of small pigmented lesions in which the distinction between melanocytic and non-melanocytic and benign and malignant lesions, and thus between melanoma and non-melanoma, is difficult or impossible to make with the naked eye. Epiluminescence microscopy is a non-invasive technique that, by use of oil immersion, makes sub-surface structures of skin accessible for *in vivo* microscopic examination and thus provides additional criteria for the diagnosis of pigmented lesions. The technique of epiluminescence microscopy is reviewed, and the significant improvement in the clinical diagnosis of pigmented skin lesions and, in particular, melanoma by this technique is documented. *J Invest Dermatol 100:356S–362S, 1993*

The history of *in vivo* skin microscopy dates back to Hinselman [1] who in 1933 proposed the use of a colposcope for high-power examination of skin and mucosal lesions and to Goldman [2] who in 1951 systematically used surface microscopy as a diagnostic procedure. Almost forgotten for 20 years and almost exclusively used for nailbed capillary microscopy [3,4], skin microscopy was revived for pigmented skin lesions (PSL) in 1971 by MacKie [5] and in 1981 by Fritsch and Pechlaner [6] who used a stereomicroscope used for ophthalmologic surgery and oil immersion in the pre-surgical evaluation of PSL. These investigators described the pigment network [6], which is now widely used as a criterion in the distinction of benign and malignant melanocytic lesions. The term *epiluminescence microscopy* (ELM) was coined by us [7,8] when we used *in vivo* surface microscopy in combination with oil immersion in a systematic analysis of the wide array of new morphologic features that become apparent by this technique. Based on the experience with over 5000 PSL, this work led to the proposal of a system of pattern analysis that eventually resulted in a significant improvement in the diagnostic score in the clinical evaluation of PSL [7,8]. The criteria used in this approach and modifications thereof are now being successfully used by a number of centers [9–12], and the results of a consensus conference on the terminology [13] and an atlas [14] have been published. This reviews the technique of ELM in PSL and documents the significant improvement in pre-surgical diagnosis by this non-invasive *in vivo* technique.

PRINCIPLE OF ELM

ELM describes the non-invasive *in vivo* examination of skin lesions with a microscope using incident light delivered from an acute angle and oil immersion. Covering the lesion with immersion oil and a glass slide that is applied with slight pressure eliminates reflectance of light from the surface and renders the stratum corneum translucent, which permits the investigator to look through the epidermis as far down as the dermoepidermal junction and, in lesions with little pigmentation, even beyond that. In other words, ELM takes *in vivo* skin microscopy one step further than surface microscopy in that it makes structures that are beyond the skin surface accessible to microscopic examination. It thus represents true, non-invasive *in vivo* microscopy of the superficial skin layers.

TECHNIQUE

ELM can be performed with binocular stereomicroscopes used as operation microscopes, for instance, in ophthalmology or plastic surgery. These microscopes are offered by several companies and provide a magnification range from $6\times$ to $80\times$. They can be equipped with an additional optical system for simultaneous viewing by a second investigator and a camera mounted on a side arm for instant photography [7]. Binocular microscopes permit high magnification, a three-dimensional appearance of the lesions, the simultaneous viewing by a second investigator, and the option of instant photography [7]. Disadvantages are size and weight of the instrument, space requirements, and costs.

ELM can also be performed with hand-held microscopes. These microscopes are monocular, small, and thus easily handled. They are equipped with an achromatic lens permitting a magnification of $10\times$. A built-in light source operates at an angle of 20° and is powered by a battery in the shaft of the instrument. This equipment is relatively inexpensive and adequate for use in clinical practice, which outweighs the limitation of low magnification and two-dimensional viewing. Hand-held equipment presently available are the dermatoscope [11,15] (Heine Delta 10; Heine Optotechnik, D-8036 Herrsching, Germany) and the episcope (Welsh and Allyn, Inc., Skaneateles Falls, NY).

PROCEDURE

Examination of a lesion by ELM involves a three-step procedure:

1. Clinical examination is done as usual and includes the analysis of the various features of a lesion by the naked eye. Criteria to differentiate melanocytic from non-melanocytic and benign from malignant pigmented lesions have been described exten sively [16–19].
2. Skin-surface microscopy uses the instrument used for ELM and provides a more detailed and subtle analysis of the criteria seen by naked eye examination, which includes the surface characteristics, configuration, color, and margins of a lesion.
3. ELM uses immersion oil and a glass slide that is pressed on the lesion in the case of large stereomicroscopes or the direct application of the hand-held instrument to the lesion. With oil immersion, the incident light is not reflected from the surface of the lesion but absorbed, scattered, and reflected from structures below the skin surface.

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Abbreviations: ELM, epiluminescence microscopy; PSL, pigmented skin lesions

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This opens a new dimension of morphologic features, colors, and patterns. ELM does consider margin, color, and configuration of a lesion, but in addition, it describes an array of new features not seen without oil immersion.

ANALYSIS

The morphology seen with ELM is new, heterogeneous, breathtakingly beautiful, but confusing for the inexperienced observer. It was therefore necessary to define morphologic features that appear regularly in different types of lesions, to create a new terminology for these features (termed *ELM criteria* [8]), and to analyze the patterns within which these criteria appear (pattern analysis [8]). Criteria are defined by purely descriptive terms that have now been correlated with histopathologic features [10,13]. Pattern analysis uses an algorithm that permits detection, analysis, and correlation of individual criteria and allows them to be placed in the context of a typical pattern for a specific pathology and thus a lesion. In other words, reading an ELM image is similar to reading a written text whereby the ELM criteria correspond to the letters of the alphabet and pattern analysis to perceiving these letters (criteria) in the context of words. ELM thus requires a process of learning.

To illustrate some of these points, the following sections describe some ELM criteria and pattern analysis as they relate to the diagnosis of pigmented lesions.

ELM CRITERIA

Pigment Network The pigment network represents a subtle network of brownish lines over a background tan (Fig 1). The anatomic basis of the pigment network is melanin pigment in the epidermal basal cells, and the holes observed in the network correspond to the tips of the dermal papillae whereby the network itself results from the projection of the pigmented rete ridges to the skin surface. The appearance of the pigment network is thus determined by size and configuration of the rete ridges, and it depends on the degree of pigmentation and the nature of the pigmented skin lesion. Basically, the pigment network may be regular or irregular, narrow or wide, delicate or prominent, and it may be well or ill denned at the margin of the lesion (Fig 2). In benign lesions, the pigment network is usually delicate, regular, and thins out at the border of the lesion, whereas in dysplastic nevi or frankly malignant lesions, it is prominent, irregular, and ends abruptly at the periphery (Fig 2). Non-me-lanocytic and amelanocytic PSL do not have a recognizable pigment network.

Diffuse Pigmentation Diffuse pigmentation that is so heavy as to preclude the recognition of a pigment network may be regular or irregular in distribution and homogenous or inhomogenous (Fig 2). In benign PSL, diffuse pigmentation, if present, is homogenous, regular, and mostly located in the center of the lesion from where it gradually fades out toward the periphery. In contrast, in dysplastic or malignant PSL, diffusely pigmented areas are inhomogenous, irregular, and may involve the periphery of the lesions (Fig 2), where they end abruptly. In other words, as in the clinical evaluation of a pigmented lesion, asymmetry of pigmentation is indicative of a dysplastic or malignant lesion also at the ELM level.

Depigmentation Depigmentation represents absence of pigment or diminution of pigment within a pigmented lesion. The term *depigmentation* as used here is always relative to the overall brown or black color of the lesion. Depigmentation may be regular or irregular and may be present in the center or the periphery of a given lesion (Fig 4). In benign PSL, depigmentation is regular and usually found in the center of the lesions, whereas in malignant PSL it is irregular and anywhere in the lesion and often found at the periphery.

Brown Globules Brown globules are round or oval, tan to dark brown spherical bodies (Fig 3*b*) that represent pigmented nevus cell nests at the junction or in the papillary dermis. They are uniform in size and regularly distributed in benign PSL (Fig 3*b)* but vary in size, color, and shape and are irregularly arranged in dysplastic or malignant PSL.

Black Dots As suggested by the descriptive term, these are small, black, punctate, or globular structures that correspond to focal accumulations of melanin pigment or pigment cells in the uppermost parts of the epidermis (Fig 3*a*). They may occur in the center, in the periphery, or throughout the PSL. When present in benign pigmented skin lesions, they only occur in the center and are regular in size, shape, and distribution. In malignant or dysplastic PSL, they also occur in the periphery of the lesion, vary in size and shape, and are irregularly distributed (Fig 3*a*).

Radial Streaming and Pseudopods Radial streaming and pseudopods are different morphologic expressions of the radial growth phase of melanoma. Radial streaming describes linear, brown to black streaks or finely serrated extensions radiating from the border of the PSL into the surrounding normal skin (Fig 5). If the lesion is not too heavily pigmented, radial streaming may also be seen within the lesion radiating either from the center or off the center of the PSL (Fig 5). As stated above, radial streaming is characteristic of superficial spreading melanoma, preinvasive or invasive, respectively. Pseudopods are also peripheral extensions of the usually heavily pigmented margin of a PSL, but in

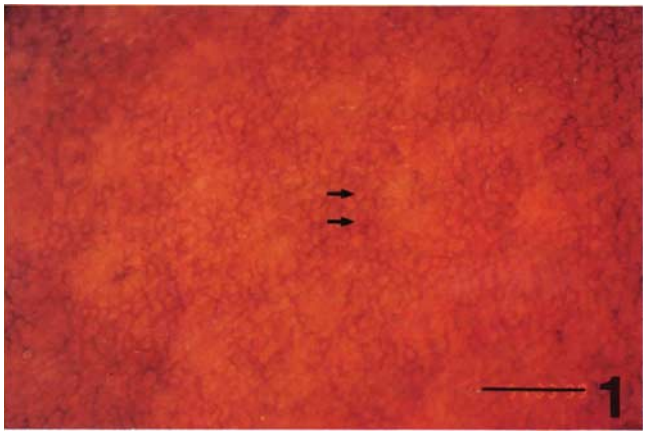

Figure 1. Pigment network in normal, type IV skin. *Arrows,* denote a network of delicate brownish lines that represent the pigmentation at the interface (e.g., the basal cell layer) of the rete pegs and dermal papillae. *Bar,* 1 mm.

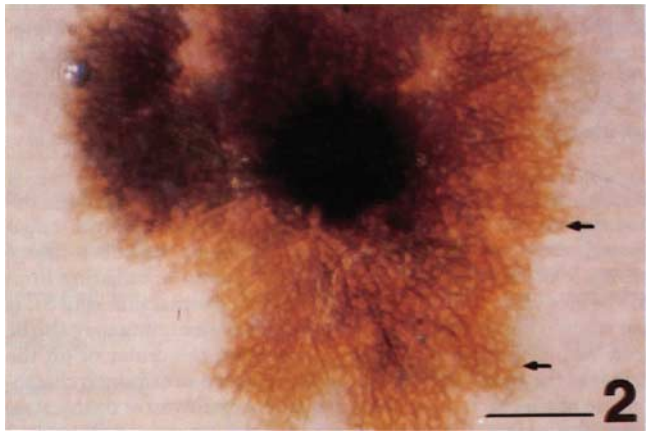

Figure 2. Pigment network in a pigmented skin lesion. The network is prominent, relatively regular throughout most of the lesion, but irregular in the left upper quadrant. It is sharply marginated at the periphery of the lesion *(arrows).* Note also that the diffuse pigmentation in the center becomes irregular and inhomogenous in the left upper quadrant. Dysplastic Nevus. *Bar,* 1 mm.

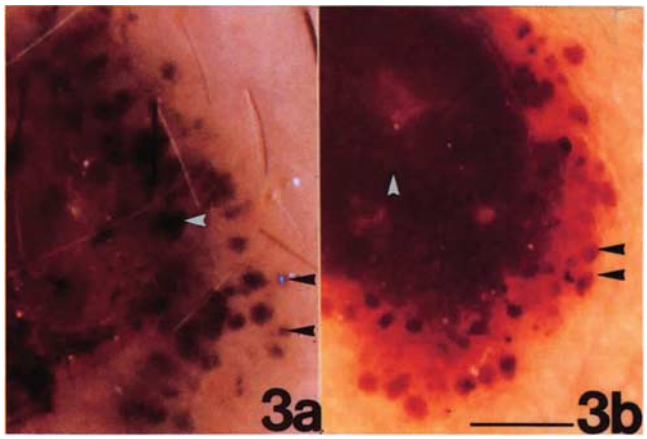

Figure 3. *(a)* Black dots *(arrowheads)* in the center and periphery of a lesion; they are of different size and the larger ones are irregular in outline. Melanoma, *(b)* Brown globules of different sizes in the periphery of a lesion *(arrowheads)*. The diffuse, heavy pigmentation in the center reveals a faint, whitish (inverted) ''pigmented network'' *(white arrow)*. Spitz's nevus. *Bar,* 0.5 mm.

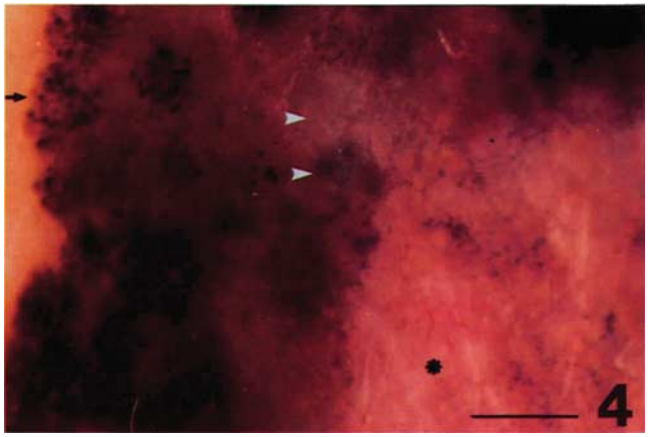

Figure 4. Depigmentation *(asterisk),* gray-blue veil *(arrowheads),* minute black dots within the depigmented area, and black dots in the periphery *(arrow)*. Superficial spreading melanoma. *Bar,* 1 mm.

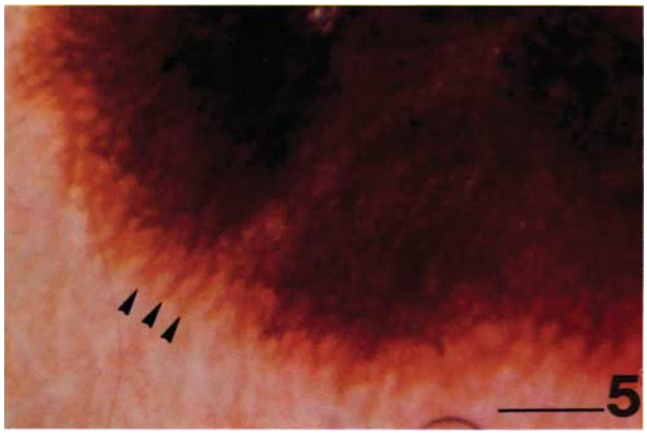

Figure 5. Radial streaming in the periphery of a PSL *(arrowheads)*. Note the serrated extensions radiating from the pigment network into the surrounding skin. Superficial spreading melanoma. *Bar,* 0.5 mm.

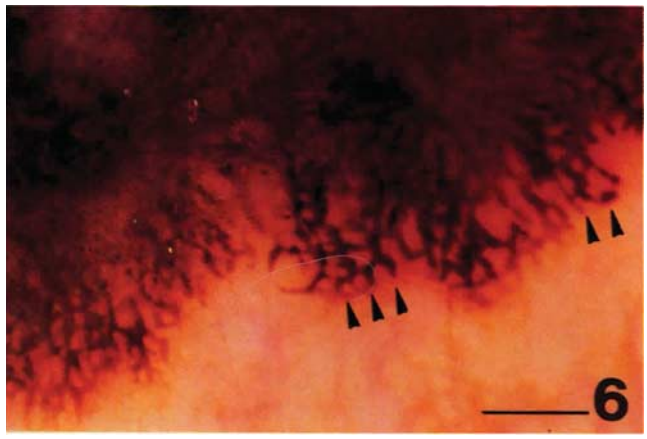

Figure 6. Pseudopods at margin of a lesion. Note kinked, finger-like extension of pigment network *(arrowheads)*. Superficial spreading melanoma. *Bar,* 0.5 mm.

Table I. ELM Criteria for Pigmented Skin Lesions

ELM Criterion	Benign PSL	Malignant PSL (melanoma)
Pigment network	Regular, delicate, narrow, gradually thins at periphery	Irregular, prominent, wide, abruptly ends at periphery
Diffuse pigmentation	Regular, homogeneous, gradually thins at periphery	Irregular, inhomogeneous, abruptly ends at periphery
Depigmentation	Regular center	Irregular center and periphery
Brown globules	Uniform in size and shape, regularly distributed	Varied in size and shape, irregularly distributed
Black dots	Uniform in size and shape, regularly distributed center	Varied in size and shape, irregularly distributed periphery
Radial streaming	Absent[a]	Present
Pseudopods	Absent	Present
Gray-blue veil	Absent	Present
Reticular depigmentation (negative pigment network)	Present[b]	Absent

[a]Except within (never peripheral) a pigmented Spitz's nevus (starburst lesion); rarely present in dysplastic nevus.
[b]Only in pigmented Spitz nevus.

contrast to radial streaming they are not linear but curved, kinked finger-like extensions of the pigment network (Fig 6). Pseudopods are almost never found in benign lesions, and their presence in PSL strongly indicates malignancy; however, not all melanomas must necessarily exhibit these features. Histologically, both radial streaming and pseudopods correspond to more or less confluent radially or more irregularly aligned globular junctional nests of melanoma cells.

Gray-Blue Veil The gray-blue veil is an ill-defined, usually irregular bluish or gray-blue area within pigmented or non-pigmented areas of PSL (Figs 4,8*b*). Histologically, it corresponds to superficial fibrosis with

Table II. Algorithm for ELM Criteria Found in PSL

ELM Criterion	Superficial Spreading Melanoma	Nodular Melanoma	Lentigo Maligna Melanoma
Pigment network	Irregular, prominent, wide, abruptly ends at periphery	Irregular, prominent, wide, abruptly ends at periphery (usually visible only as peripheral rim)	Highly irregular, prominent, abruptly ends or thins at periphery
Diffuse pigmentation	Irregular, inhomogeneous, abruptly ends at periphery	Irregular, inhomogeneous, abruptly ends at periphery	Irregular, inhomogeneous, abruptly ends or thins at periphery
Depigmentation	Irregular, bizarre, pink-and-white center and periphery	Irregular, bizarre, pink-and-white center and periphery	Irregular, bizarre, pink-and-white center and periphery
Brown globules	Often present, varied in size and shape, irregularly distributed	Rarely present, varied in size and shape, irregularly distributed	Rarely present, varied in size and shape, irregularly distributed
Black dots	Often present, varied in size and shape, irregularly distributed periphery and center	Often present, varied in size and shape, irregularly distributed periphery	Often present, varied in size and shape, irregularly distributed, periphery and center
Radial streaming	Present	Present	Present
Pseudopods	Present	Present	Rarely present
Gray-blue veil	Present	Present	May be present

ELM Criterion	Lentigo Maligna Melanoma *In situ*	Lentigo Simplex, Nevoid Lentigo
Pigment Network	Irregular, prominent, wide, abruptly ends or thins at periphery	Regular, periphery prominent, narrow, gradually thins at periphery
Diffuse Pigmentation	Irregular, inhomogeneous, abruptly ends at periphery	Regular, homogeneous center
Depigmentation	Irregular, bizarre, pink-and-white center and periphery	Absent
Brown globules	Rarely present, varied in size and shape, regularly distributed	Absent
Black dots	Rarely present, varied in size and shape, irregularly distributed	Absent
Radial streaming	Present	Absent
Pseudopods	Absent	Absent
Gray-blue veil	Absent	Absent

ELM Criterion	Dysplastic Nevus	Junctional Nevus	Dermal Nevus	Compound Nevus
Pigment network	Irregular, discrete, focally prominent, abruptly ends or thins at periphery	Regular, prominent, thins at periphery	Absent	Regular, discrete, thins at periphery
Diffuse pigmentation	Irregular, intense, inhomogeneous, center, periphery abruptly ends at periphery	Regular, intense, homogeneous center thins at periphery	Regular, faint, homogeneous throughout lesion, thins at periphery	Regular, faint homogeneous center and periphery, thins at periphery
Depigmentation	Irregular, periphery	Absent	Regular, center	Regular center and periphery
Brown globules	Varied in size and shape, irregularly distributed	Rare, uniform in size and shape, regularly distributed	Absent	Uniform in size and shape, regularly distributed
Black dots	Rare, regularly distributed throughout lesion	Rare, regularly distributed center	Absent	Very rare, regularly distributed center
Radial streaming	Absent (very rarely present)	Absent	Absent	Absent
Pseudopods	Absent	Absent	Absent	Absent
Gray-blue veil	Absent	Absent	Absent	Absent

ELM Criterion	Pigmented Spitz Nevus	Blue Nevus
Pigment network	Regular, very prominent, abruptly ends at periphery	Absent
Diffuse pigmentation	Regular, intense, inhomogeneous center and periphery, abruptly ends at periphery	Regular, intense steel blue, homogeneous throughout lesion, abruptly ends at periphery
Depigmentation	Regular, irregular reticular depigmentation (negative pigment network) center	Absent
Brown globules	Uniform in size and shape; regularly distributed, forming rim around lesion	Absent
Black dots	Uniform in size and shape, regularly arranged throughout lesion	Absent
Radial streaming	Absent	Absent
Pseudopods	Absent	Absent
Gray-blue veil	Absent	Absent

Table III. Patterns in Non-Melanocytic Pigmented Lesions

ELM Criterion	Angioma	Pigment Basal Cell Carcinoma	Seborrheic Keratosis
Pigment network	Absent	Absent	Absent
Diffuse pigmentation	Absent	Irregular, inhomogeneous, thins at periphery	Regular, homogeneous, abruptly ends at periphery
Depigmentation	Absent	Irregular center and periphery	Absent
Brown globules	Absent	Absent	Absent
Black dots	Absent	May be present	Absent
Radial streaming	Absent	Absent	Absent
Pseudopods	Absent	Absent	Absent
Gray-blue veil	Absent	May be present	Absent
Others	Reddish-blue lacunes, extremely sharply defined	Teleangiectasia	Horny cysts, keratotic plugs

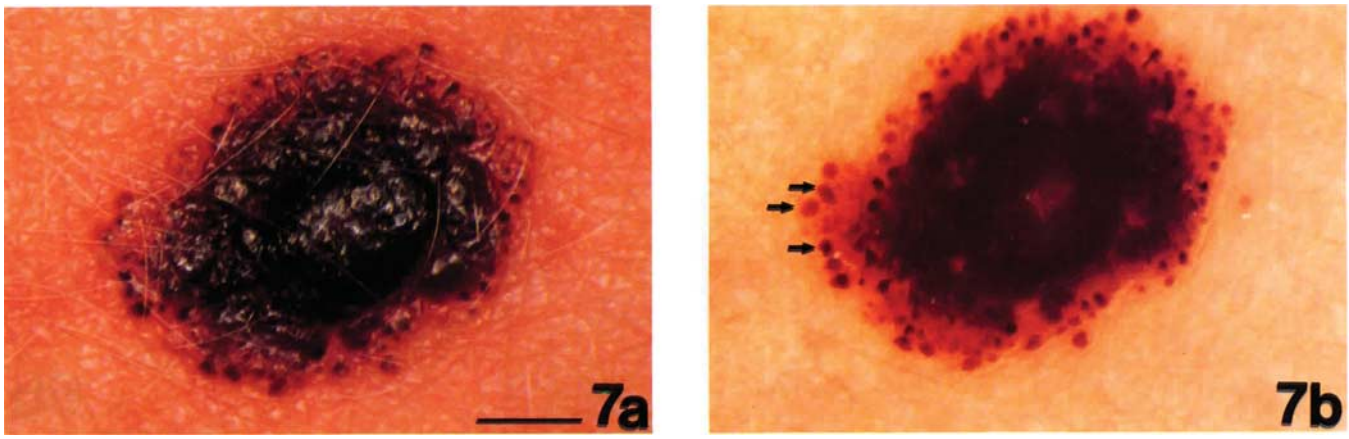

Figure 7. *(a)* Small, heavily pigmented, slightly irregular PSL with satellite pigmented nodules at periphery. Surface microscopy without oil immersion. The lesion could be a melanoma, a common acquired or small congenital nevus, or a pigmented Spitz nevus. *Bar,* 1 mm. *(b)* ELM of the same lesion reveals a rim of regular brown globules in the periphery *(arrows)* and within the central, diffuse pigmentation an area of depigmentation and a faintly visible inverted pigment network. Radial streaming, pseudopods, and peripheral black dots are absent. The diagnosis is thus pigmented Spitz' nevus. (Magnification as in Fig 7a.)

melanophages and/or (malignant) pigment cells in the papillary dermis. This is also almost exclusively found in malignant melanoma in areas of regression but may be seen in pigmented basal cell carcinoma.

Retkular Depigmentation or Negative Pigment Network: This represents an inverse pigment network with a whitish net against a dark, pigmented background (Fig 3*b*). This reticular depigmentation is almost exclusively found in a pigmented Spitz' nevi.

For reasons of brevity, not all criteria elaborated over the past years are described here, but those that are relevant for PSL can be found in Table I. It should also be emphasized that these criteria can be seen in the center or near the center of a pigmented skin lesion only if overall pigmentation is not so heavy as to obscure these features. In the latter case, such criteria can be detected only on the margin of a lesion or not at all.

PATTERN ANALYSIS

Pattern analysis of now over 7000 pigmented skin lesions has permitted a compilation and listing of criteria that are commonly found in and are thus typical for various types of PSL [7]. This, then, provides algorythms that define patterns of criteria characteristic for such lesions (Table I). Table II gives examples of patterns typical of different types of PSL; to contrast this, Table III lists patterns not described in detail in this review but published elsewhere [7,8] that are encountered in non-melanocytic pigmented lesions. It is apparent that comparison of these patterns allows not only differentiation of melanocytic from non-melanocytic pigmented lesions but also, insofar as melanocytic pigmented lesions are concerned, the ability to distinguish between benign and malignant growth patterns. Figures 7 and 8 illustrate this point: Both lesions shown are small, heavily pigmented, and irregular. Magnification by surface microscopy only enhances the impression gained by visual examination (Figs 7*a* and 8*a*) whereas ELM (Figs 7*b* and 8*b*) reveals criteria that by pattern analysis yield the correct diagnosis.

Our experience with pattern analysis has made us realize several rules that should be observed when PSL are examined by ELM:

(1) The presence of a criterion is more important than its absence;
(2) one single criterion usually does not suffice to make a diagnosis;
(3) some criteria are more important than others (e.g., radial stream ing, pseudopods, and gray-blue veils distinguish specifically be tween dysplastic nevi and radial growth phase of melanoma); and
(4) the absence of defined criteria (i.e., their non-visibility due to heavy, overall pigmentation) does not permit an ELM diagnosis.

QUANTITATIVE EVALUATION OF CRITERIA FOR EPILUMINESCENCE MICROSCOPY

To be useful for clinical diagnosis, the ELM criteria described above had to be weighted according to their significance in the diagnosis of PSL. In a recent study (A. Steiner *et al,* unpublished observations), 191 melanocytic PSL were investigated by ELM using a Wild M650 binocular surface microscope, and the variables of the standard ELM criteria were assessed for each lesion. After ELM examination, all PSL were excised and processed for histopathology. Using descriptive statistical methods, including the chi-square test, the following of the criteria described above were found to be highly significant in the discrimination of common from dysplastic nevi: type of pigmentation, regular discrete pigment network, and a gradually thinning margin of the pigment network at the periphery. By differentiating dysplastic nevi from melanomas, we found the following criteria to be highly significant: irregular, discrete pigment network; abrupt break-off of the pigment network margin; irregular depigmentation at the periphery; pseudopods; radial streaming; and irregularly distributed black dots at the periphery of lesions. ELM criteria thus have different weights of significance in the differential diagnosis of melanocytic pigmented skin lesions. Selection of patterns of criteria adjusted to the distinct type of PSL therefore promises to considerably improve the diagnostic accuracy of melanocytic PSL by ELM.

DIAGNOSTIC SIGNIFICANCE OF ELM IN THE DIAGNOSIS OF PIGMENTED SKIN LESIONS USING ELM PATTERN ANALYSIS

To prove or disprove the value of ELM pattern analysis in the diagnosis of pigmented skin lesions, ELM studies were performed on small (<0.5 cm) pigmented skin lesions that were diagnostically equivocal when examined with the naked eye. In an initial investigation, an improvement of clinical diagnosis was achieved by ELM for practically all lesions, benign and malignant, and was equally impressive for melanocytic and non-melanocytic lesions [8]. This study has now been extended to 509

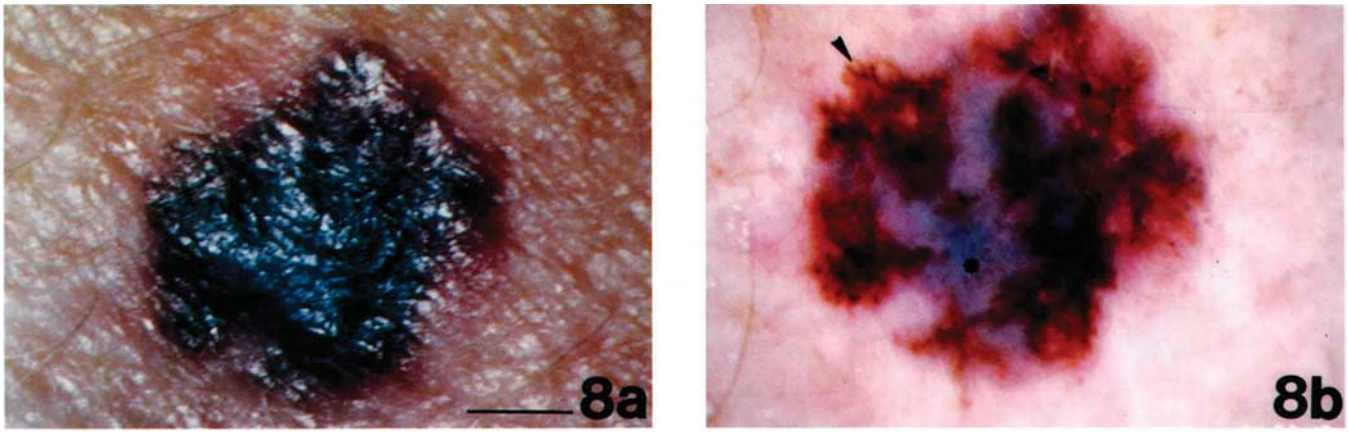

Figure 8. *(a)* Small irregular, heavily pigmented lesion as seen by surface microscopy without oil immersion. This lesion could be a pigmented basal cell carcinoma, an irregular common nevus or a melanoma. *Bar,* 1 mm. *(b)* ELM of the same lesion reveals an irregular pigment network with radial streaming *(arrowhead),* a gray-blue veil *(asterisk),* and irregular pigmentation. The lesion is a superficial spreading melanoma. (Magnification as in Fig 8a.)

Table IV. Improvement of Clinical Diagnosis of PSL by ELM

Histologic Diagnosis	Number of Lesions	Number of Clinical Diagnoses Correct (%)	Number of ELM Diagnoses Correct (%)
Junctional nevus	48	35 (73%)	40 (83%)
Blue Nevus	34	22 (65%)	30 (88%)
Spitz nevus (pigmented)	54	30 (56%)	50 (93%)
Dysplastic nevus	145	85 (59%)	110 (76%)
Lentigo simplex/nevoid lentigo	21	10 (48%)	14 (67%)
Lentigo maligna (melanoma)	20	14 (70%)	16 (80%)
Superficial spreading melanoma *in situ*	30	15 (50%)	25 (83%)
Superficial spreading melanoma, invasive	69	37 (54%)	63 (91%)
Nodular melanoma	13	6 (46%)	8 (62%)
Seborrheic keratosis	26	16(62%)	20 (77%)
Basal cell carcinoma	31	18 (58%)	26 (84%)
Angioma/angiokeratoma	18	15 (83%)	18 (100%)
Total	509	303 (60%)	420 (84%)

small (<0.5 cm) pigmented skin lesions by using an identical study protocol. Briefly, the large majority (>80%) of the 509 lesions were found to be diagnostically equivocal in that there was no complete agreement on the clinical diagnosis among three investigating clinicians. All lesions had been independently seen and diagnosed by three investigators, and the diagnosis that appeared as the most likely one to at least two of the three investigators was provisionally recorded as clinical diagnosis. Even in those cases where concordance of diagnosis among the three investigators was achieved, at least one of the investigators was not absolutely sure whether his diagnosis was correct. The same lesions were then subjected to ELM pattern analysis, as described. The ELM diagnosis, again made independently by the three investigators, on which at least two of the three investigators agreed was recorded as the final ELM diagnosis. All lesions were then excised and subjected to histopathologic examination in subserial sections. Clinical, ELM, and histopathologic diagnosis were eventually compared for each lesion, and the correlation of the diagnostic reliability was established. Figures 7 and 8 show two examples of the types of lesions examined, and Table IV summarizes the overall results of this study. Again, it is obvious that an improvement in the accuracy of clinical diagnosis was achieved by ELM pattern analysis for nearly all lesions. Particularly impressive is the improvement in the diagnostic score achieved for dysplastic nevi, superficial spreading melanoma *in situ,* superficial spreading melanoma (invasive), and pigmented basal cell carcinoma (Table IV). It should be noted, however, that even exact pattern analysis does not completely eliminate diagnostic errors and that ELM thus does not provide 100% diagnostic accuracy.

DISCUSSION

There is consensus that the impressive 5-year survival rate for 80–90% of melanomas diagnosed in experienced centers is solely attributable to early diagnosis [20]. At the same time, it is disconcerting that even in specialized centers, the diagnostic accuracy for early malignant melanoma is only 64% [21], and this considerably dims the hope that even earlier clinical detection of this tumor will considerably reduce mortality. ELM has the potential to correct these diagnostic limitations in that it permits the recognition of malignant pigmentary lesions much earlier than by clinical inspection alone. The fact that it is a non-invasive *in vivo* method makes it even more attractive as a diagnostic tool in clinical practice. We have shown in this article that ELM 1) helps to distinguish between melanocytic and non-melanocytic lesions; 2) that it helps to distinguish between benign and malignant growth patterns of pigmented lesions; and 3) that it decisively improves the diagnostic score for pigmented lesions and thus melanoma.

ELM also has its limitations: It does not provide 100% diagnostic accuracy; it is of little help in small, maximally pigmented lesions that do not reveal the criteria necessary for ELM pattern analysis; and it therefore does not replace histopathology. Nonetheless, ELM has already proved to be of great practical value in several centers by increasing the probability that an early melanoma is not missed and by helping to prevent unnecessary major surgery in those cases where non-melanocytic or benign PSL are clinically suspected to be melanoma. For example, in a study of 318 PSL published previously [8], 16 lesions clinically diagnosed as melanoma were recognized as dysplastic nevi (12) and Spitz's nevi (4) by ELM. Perhaps most important, ELM may eventually prove invaluable for patients with dysplastic nevi, where it may aid in the decision as to which lesions need to be removed and which do not. This, however, will have to be proved in formal studies.

There is no doubt that the method will have to be improved, and only continued studies will show how reliable the individual criteria discussed in this review will prove to be in even larger cohorts of patients. There is also no doubt that methods will have to be found to make pattern analysis more objective. One approach to the solution of this problem is computerized imaging of ELM, which, in addition, will provide unlimited capacity for data storage and retrieval. Studies in this direction are underway.

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