Digital computer analysis of dermatoscopy images of 260 melanocytic skin lesions: perimeter/area ratio for the differentiation between malignant melanomas and melanocytic nevi

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Keywords
computer analysis, dermatoscopy, malignant melanoma, perimeter/area ratio

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Abstract

Background Digital computer analysis of dermatoscopy images has been reported to facilitate the differential diagnosis of pigmented skin lesions in recent years.

Objective The aim of our study was to perform digital computer analysis of a set of different melanocytic lesions and compare the objective results.

Methods The set of 260 melanocytic lesions (150 excised difficult cases (46 melanomas, 47 atypical nevi, 57 common nevi and 110 unexcised common nevi) was automatically analysed by the digital dermatoscopical system microDERM. We searched for differences in asymmetry, size, compactness and colour distribution. Perimeter/area ratio was calculated.

Results The perimeter/area ratio was detected as the most important criterion for differentiation between malignant and benign melanocytic lesions (sensitivity 91.3% and specificity 90.7% for malignant melanomas vs. all benign nevi; sensitivity 91.3% and specificity 80.8% for melanomas vs. clinically atypical nevi). Differences in size of the lesion, shape and asymmetry of colour were found and statistically verified. Using step-wise logistic regression the formula for calculation of probability of malignant nature of every analysed lesion was constructed.

Conclusion The perimeter/area ratio is a simple parameter for the differential diagnosis of melanocytic skin lesions.

Introduction

The incidence and mortality rates of cutaneous malignant melanoma (MM) have risen in the past decades. The prognosis for advanced MM remains poor. However, if detected during the earliest stages, MM can be successfully treated. Early detection of MM by means of accurate screening is an important step towards reduction in mortality and prolongation of patients’ survival. Despite extensive research, the clinical diagnostic accuracy of MM remains difficult in many cases, even in specialized dermatological centres. An accurate clinical skin examination by experienced dermatologist remains the basic diagnostic procedure for the differential diagnosis of pigmented and non-pigmented skin lesions. Several in vivo diagnostic methods have been introduced to clinical practice, among which dermatoscopy is the most important. This method makes the subsurface structures of the skin visible and enhances the colour resolution. Dermatoscopy offers to the clinician improvement in the quality of differential diagnosis of pigmented skin lesions and reduction of unnecessary surgical procedures. However, even with the use of dermatoscopy MM, and particularly early MM, cannot always be differentiated from benign melanocytic skin lesions with certainty. Advances in computer technology and digital imaging have been applied to explore their
potential use in the evaluation of pigmented skin lesions. The digital form of dermoscopy allows the physician storage, comparison and analysis of digital dermatoscopical images. By use of modern software, digital computer analysis of dermatoscopical images is possible. Geometric, structural and colour features of examined lesions can be objectively evaluated; some computers even determine the definite diagnosis. Several studies have already confirmed the efficacy of digital computer analysis of dermatoscopical images for the diagnosis of melanocytic skin lesions. However, the clinical application of this method in daily practice has not been clarified. The aim of our study was to evaluate the possible differences observed by using digital computer analysis of dermatoscopical images of melanocytic skin lesions, especially those where the clinical differential diagnosis between MM and benign melanocytic nevus was difficult. We used the digital dermatoscopical device microDERM and its software (based on the DANAOS system – diagnostic and neural analysis of skin cancer system) for computer analysing.

Material and methods
The digital dermatoscope microDERM (Visioderm Comp., Bochum, Germany), comprising a hand-held video camera and image acquisition computer system, was used for dermatoscopical examinations for the purposes of the study. All lesions were recorded and then stored in a computer under standardized conditions at magnifications corresponding best to the size and shape of every lesion (15-, 20-, 30-, 50-fold) by the use of immersion. The hand-held unit of the dermatoscopical device contained a miniaturized CCD camera, optical lens system and a light source. The illumination was realized by white light-emitting diodes (LEDs) placed inside the unit. Selected images were analysed by the neural network analytic system, a component of the microDerm device. The analytic process starts with segmentation, where the outer border of the selected lesion has to be determined. This step has to be visually controlled. A hybrid method that combines a statistical clustering of the colour space and a hierarchical region-growing algorithm was used for border detection. After segmentation, the feature extraction process was concentrated directly on the lesion. The analytic software version of microDERM presented the results following ‘ABCD criteria’. The ‘asymmetry percentage’ was estimated first by finding the principal axes of inertia (A1, A2) of the lesion, then by computing the non-overlapping areas after an imaginary ‘folding’ operation along these axes, divided finally by the total area of the tumour. In the ‘border domain’, perimeter (mm), area (mm²) and compactness index of the lesion were measured or calculated. The compactness describes the deviation of the examined lesion’s real shape from the circle. The ideal circle has a compactness index of 1: the higher the index is the greater the shape deviation is. We calculated the perimeter/area ratio (1/ mm) by dividing both appropriate parameters as a possible characteristic of the arrangement of demarcation of the examined lesion. The ‘variation in colour’ was expressed by the variance of red, green and blue colour components (0–1 maximum). The calculation of colour asymmetry along both axes was presented graphically in a colour scale (bright colours served as an indicator of the sources of colour asymmetry inside the lesion – ‘hot spots’). The diameters on both axes of symmetry were measured in mm.

Three hundred and five digital dermatoscopical images of melanocytic skin lesions were selected for digital analysis. All lesions were examined by the naked eye and by the digital dermatoscopical system. One hundred and eighty lesions were excised owing to clinical and/or dermatoscopical features suspected as characteristic of a highly atypical melanocytic nevus or MM, and histopathologically examined. All procedures were carried out at the department of dermatology of the Charles University Hospital in Pilsen, the Czech Republic between January 2002 and December 2004. In addition, the set of 125 non-excised benign melanocytic nevi not suspected as malignant were added for the purposes of the study. These 125 lesions were examined in the group of patients followed up for multiple benign melanocytic nevi. Lesions located on the face, palms and soles, subunqual and mucosal sites were not included.

We considered all studied lesions as 1/clinically atypical and histologically common benign melanocytic nevi, 2/ clinically and histologically atypical benign melanocytic nevi, 3/malignant melanomas, or 4/non-excised clinically common benign melanocytic nevi. The results of digital computer analysis of dermatoscopical images were compared for these categories of melanocytic lesions. All lesions were flat or only slightly elevated, hairless, and 2.5–14.5 mm in diameter. The whole lesion was always seen on the screen when dermatoscopically examined. On clinical examination, melanocytic nevus was defined as atypical only if at least two of the additional following attributes were present: asymmetry, irregular border, and variegation of colour. Common nevi did not fulfill these clinical criteria. On histological examination, melanocytic nevi were defined as atypical only if they had all of the following histological features: (1) architectural atypia (peripheral extension of junctional component beyond dermal component); (2) lentiginous hyperplasia (proliferation of melanocytes along the basal layer); (3) cytological atypia (some cells had hyperchromatic nuclei and prominent nucleoli); and (4) stromal response (fibroplasia of papillary dermis). The diagnosis of MM was confirmed by histopathology in all cases, and Breslow’s thickness was measured.
Computer analysis of melanocytic lesions

The results of digital computer analysis were compared for all listed categories of melanocytic lesions. The differences between melanomas vs. all benign lesions and melanomas vs. clinically atypical melanocytic nevi were monitored. The average values and standard deviations were calculated for all parameters. All results were statistically verified. The Chi-square test was used for the criterion of colour asymmetry; Wilcoxon’s unpaired test was used for monofactorial comparison of all other criteria. Finally, multifactorial analysis (logistic step-wise regression test) was performed.

Results

Forty-five cases were excluded from the analysis of dermatoscopy images of melanocytic skin lesions (nine MM, eight histologically atypical nevi, 13 histologically common nevi and 15 non-excised nevi). An inaccurate determination of the border of an analysed lesion was the reason for exclusion in all cases, because the MiDROEM system does not offer the possibility of manual correction of boundary detection. Digital computer analysis of the remaining 260 dermatoscopy images of melanocytic skin lesions (150 excised, 110 non-excised) was successfully completed and these cases were finally included in the study. Of 150 excised and histopathologically examined lesions, 46 were considered as MM (13 MM in situ, 33 invasive melanomas, with mean Breslow’s thickness of 0.77 mm), 47 lesions were both clinically and histopathologically atypical melanocytic nevi and 57 clinically atypical nevi were histopathologically considered as common nevi. Another 110 clinically common melanocytic nevi used in this study were not excised.

All results of digital computer analysis are summarized in Table 1. Malignant melanomas were more asymmetric than benign melanocytic nevi were ($P < 0.001$ for A1 axis, $P < 0.01$ for A2 axis); atypical nevi were more asymmetric than common nevi. Malignant melanomas were larger in size when comparing the same parameters (perimeter, area, maximal diameter) than benign lesions ($P < 0.001$); these values were again higher for atypical than for common nevi.

Perimeter/area ratio was calculated for all analysed cases as an extra characteristic of demarcation of the lesion. We found significant differences when comparing malignant and benign lesions ($P < 0.001$). The mean value of perimeter/area ratio of all MMs was 0.8084 (0.4833–1.4088) vs. 1.6431 (0.5330–3.9623) of all benign lesions; for clinically and histologically atypical nevi it was 1.1903 (0.5330–2.2660), for clinically atypical and histologically common nevi, 1.5820 (0.9279–3.2325), and for non-excised common melanocytic nevi, 1.8780 (1.0009–3.9623) (fig. 1).

We found differences in this parameter also when comparing only melanomas 0.8084 (0.4833–1.4088) and clinically atypical nevi 1.3806 (0.5330–2.3653), so only difficult to diagnose lesions. We tried to use perimeter/area ratio to discriminate between MM (below the value of 1) and melanocytic nevi (over the value of 1) of our set. We achieved a sensitivity of 91.3% and specificity of 90.7% for MM vs. all benign nevi; and sensitivity of 91.3% and specificity of 80.8% if only clinically atypical nevi were considered as benign lesions. Perimeter/area ratio was over the value of 1 only in four cases of MM (false negatives), vs. in 194 cases of benign melanocytic nevi (true negatives). Five lesions were diagnosed histologically as common nevi and 15 lesions as atypical nevi in the group of 20 false-positive cases. No common non-excised nevus showed a perimeter/area ratio below the value of 1.

The compactness of the examined lesion was not useful for differentiation between benign and malignant tumours, as the numeric value of index of compactness did not correlate with the lesion type ($P > 0.05$ for MM vs. atypical nevi). The numeric values of colour variation also did not serve as possible an indicator of malignancy ($P > 0.05$ for MM vs. atypical nevi). We did not observe useful differences between MM and melanocytic nevi; the variance for red colour was non-significantly higher in MM than in nevi, the variance values for green and blue colour were even higher in benign lesions. It is difficult to evaluate the results of colour asymmetry analysis, which are graphically presented. ‘Hot spots’ are areas of different colours, which serve as the sources of colour asymmetry. They are identified by computer analysis as bright colours along both axes of symmetry. The presence vs. absence of colour asymmetry differed significantly between MM and nevi ($P < 0.001$). Colour asymmetry (‘hot spots’) was detected in 95.7% of MM (in 69.6% along both axes), while more than a half of all nevi (51.4%) showed complete absence of colour asymmetry.

The criteria asymmetry A1 axis, perimeter, area, perimeter/area ratio, maximal diameter, colour asymmetry, and asymmetry A2 axis were found to be statistically significant for differentiation between MM and clinically atypical melanocytic nevi (also MM vs. all nevi) in our study. Finally, multifactorial statistical analysis of presented results was performed. The logistic step-wise regression test found two parameters (perimeter/area ratio and asymmetry A1 axis) to be the most important for differentiation between malignant melanomas and clinically atypical nevi (or all benign nevi). On the basis of statistical analysis the following formula for calculation of the probability of malignant nature of every analysed lesion can be constructed:

$$P = 1[1 + \exp(-4.738 + 7.474 \times \text{RATIO} - 0.190 \times \text{ASYM1})]$$

where $P$ = probability of malignant character of lesion, RATIO = perimeter/area ratio of lesion and ASYM1 = asymmetry of lesion along A1 axis.
## Table 1 Results of digital computer analysis of melanocytic skin lesions

<table>
<thead>
<tr>
<th></th>
<th>Malignant melanomas</th>
<th>All clinically atypical excised nevi</th>
<th>All benign melanocytic nevi</th>
<th>Clinically atypical excised nevi</th>
<th>Histologically atypical nevi</th>
<th>Histologically common nevi</th>
<th>Non-excised common nevi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymmetry (%) A1 axis</td>
<td>11.6293 (SD ± 3.9287)</td>
<td>*8.9248 (SD ± 4.0783)</td>
<td>*8.5834 (SD ± 3.4336)</td>
<td>10.1600 (SD ± 4.3967)</td>
<td>7.9063 (SD ± 3.4804)</td>
<td>8.2635 (SD ± 2.6533)</td>
<td></td>
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<tr>
<td>Asymmetry (%) A2 axis</td>
<td>8.5699 (SD ± 3.4425)</td>
<td>*7.0030 (SD ± 3.1018)</td>
<td>**6.8205 (SD ± 2.7052)</td>
<td>7.4683 (SD ± 3.0360)</td>
<td>6.6194 (SD ± 3.1031)</td>
<td>6.6495 (SD ± 2.2583)</td>
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<tr>
<td>Perimeter (mm)</td>
<td>43.8029 (SD ± 11.1392)</td>
<td>*30.6431 (SD ± 13.4812)</td>
<td>*29.1390 (SD ± 14.1664)</td>
<td>35.6288 (SD ± 13.9660)</td>
<td>25.4469 (SD ± 11.2312)</td>
<td>27.6129 (SD ± 14.6400)</td>
<td></td>
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<tr>
<td>Area (mm²)</td>
<td>56.5362 (SD ± 21.4963)</td>
<td>*26.1784 (SD ± 16.9283)</td>
<td>**21.6806 (SD ± 15.6815)</td>
<td>33.8018 (SD ± 19.3548)</td>
<td>18.0159 (SD ± 10.9245)</td>
<td>17.4272 (SD ± 13.0806)</td>
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<tr>
<td>Perimeter/area ratio (1/mm)</td>
<td>0.8084 (SD ± 0.1950)</td>
<td>*1.3806 (SD ± 0.4665)</td>
<td>*1.6431 (SD ± 0.6222)</td>
<td>1.1903 (SD ± 0.3569)</td>
<td>1.5820 (SD ± 0.4965)</td>
<td>1.8780 (SD ± 0.6486)</td>
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<tr>
<td>Compactness index</td>
<td>2.8378 (SD ± 0.7554)</td>
<td>3.2099 (SD ± 1.3811)</td>
<td>**3.6052 (SD ± 1.6175)</td>
<td>3.2655 (SD ± 1.3608)</td>
<td>3.1306 (SD ± 1.3926)</td>
<td>3.9955 (SD ± 1.7312)</td>
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<tr>
<td>Colour variation index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Red</td>
<td>0.2371 (± 0.1152)</td>
<td>†0.2361 (± 0.1119)</td>
<td>0.2237 (± 0.1041)</td>
<td>0.2172 (± 0.1122)</td>
<td>0.2498 (± 0.1098)</td>
<td>0.2111 (± 0.0949)</td>
<td></td>
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<tr>
<td>Green</td>
<td>0.1134 (± 0.0818)</td>
<td>†0.1420 (± 0.0959)</td>
<td>**0.1758 (± 0.0832)</td>
<td>0.1181 (± 0.0815)</td>
<td>0.1611 (± 0.1025)</td>
<td>0.1723 (± 0.0832)</td>
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<tr>
<td>Blue</td>
<td>0.0247 (± 0.0493)</td>
<td>†0.0409 (± 0.0606)</td>
<td>***0.0516 (± 0.1014)</td>
<td>0.0313 (± 0.0453)</td>
<td>0.0491 (± 0.0697)</td>
<td>0.0622 (± 0.1276)</td>
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<tr>
<td>Colour asymmetry (%)</td>
<td></td>
<td>(P &lt; 0.001)</td>
<td>(P &lt; 0.001)</td>
<td></td>
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<tr>
<td>Both axes positive</td>
<td>32 cases (69.6%)</td>
<td>33 cases (31.7%)</td>
<td>48 cases (22.4%)</td>
<td>17 cases (36.2%)</td>
<td>16 cases (28.1%)</td>
<td>15 cases (13.6%)</td>
<td></td>
</tr>
<tr>
<td>One axis positive</td>
<td>12 cases (26.1%)</td>
<td>37 cases (35.6%)</td>
<td>56 cases (26.2%)</td>
<td>20 cases (42.6%)</td>
<td>17 cases (29.8%)</td>
<td>19 cases (17.3%)</td>
<td></td>
</tr>
<tr>
<td>No hot spots present</td>
<td>2 cases (4.3%)</td>
<td>34 cases (32.7%)</td>
<td>110 cases (51.4%)</td>
<td>10 cases (21.3%)</td>
<td>24 cases (42.1%)</td>
<td>76 cases (69.1%)</td>
<td></td>
</tr>
<tr>
<td>Maximal diameter (mm)</td>
<td>9.2418 (SD ± 2.0211)</td>
<td>*6.2338 (SD ± 2.0711)</td>
<td>*5.6566 (SD ± 2.0597)</td>
<td>7.0212 (SD ± 2.1533)</td>
<td>5.4102 (SD ± 1.6759)</td>
<td>5.0871 (SD ± 1.8956)</td>
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</tr>
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</table>

Results of single parameters differ to the significance level of 1 per mille (P < 0.001), 1% (**P < 0.01), 5% (***P < 0.05) or were found as statistically non-significant (†P > 0.05) for differentiation between selected type of benign lesions (atypical nevi or all benign nevi) and malignant melanomas.

The Chi-square test was used for colour asymmetry; Wilcoxon's unpaired test was used for all other criteria.
The efficacy of this formula was controlled for melanomas vs. atypical nevi (84.7% of correct predictions) and melanomas vs. all nevi (89.3% of correct predictions).

**Discussion**

Early recognition followed by surgical excision remains the basic medical approach for patients with MM. Dermatoscopy as an *in vivo* non-invasive diagnostic method provides an additional view on examined pigmented skin lesions and additional criteria for making the correct diagnosis. Digital dermatoscopy offers new dimensions of this diagnostic procedure. Data from several studies suggest that dermatoscopy can increase the sensitivity and specificity for the clinical detection of MM and some lesions that frequently mimic MM. Dermatoscopical classifications, algorithms or tests, as well as digital analytical methods have been investigated to facilitate the differential diagnosis of difficult cases.  

Four different algorithms of conventional dermatoscopy are frequently used to differentiate MM from benign melanocytic lesions: modified pattern analysis, ABCD rule of dermatoscopy, 7-point checklist and Menzies’ method. Within the framework of the Consensus Net Meeting on Dermatoscopy results of these diagnostic procedures have been re-evaluated and compared. The sensitivity varied between 82.6 and 85.7%, and the specificity between 70 and 83.4% for distinguishing MM from benign lesions. Pattern analysis allowed the best diagnostic performance. Several attempts to compare the results of digital dermatoscopical analysis of MM and nevi have already been made in the 1990s. Andreassi stated the necessity of transformation of images into numbers to become objective results. The efficacy of digital dermatoscopical analysis for the differential diagnosis of melanocytic lesions has been repeatedly confirmed. Piccolo *et al.* reported the sensitivity of digital computer analysis as comparable to that obtained by an experienced dermatologist using the conventional technique of dermatoscopy; the specificity of digital analysis was significantly lower. In general, diagnostic accuracy of digital computer analysis is published as comparable to the conventional algorithms used by experienced dermatoscopists.

The aim of our work was not to re-evaluate the diagnostic accuracy of digital dermatoscopical analysis, which has been already done; in fact, with the same instrument as we used for the purposes of this study. We tried to compare frequently used ABCD criteria of different types of melanocytic skin lesions when automatically calculated by the use of computer image analysis.

A well-known parameter for distinguishing between malignant and benign melanocytic nevi is simply the size of the lesion (perimeter, area and diameter), even when comparing difficult cases. MM were also larger than nevi in our study. We constructed perimeter/area ratio as a simple parameter to characterize the arrangement of the border of examined melanocytic lesions. We found perimeter/area ratio as the most significant and simply calculated criterion for differentiation between MM and benign melanocytic nevi in our study. The sensitivity and specificity of this algorithm for discrimination between MM and melanocytic nevi are comparable to those of generally respected methods, even in clinically difficult cases. It is a well-known fact that the pigment network of melanocytic nevi fades gradually, with many thin, regular extensions into the adjacent healthy skin at the periphery. The margin of melanocytic nevus detected by computer is mostly lappeted. The situation is frequently opposite in superficial spreading MM, where the cut-off extensions of atypical pigment networks or short and thick pseudopods are registered at the periphery. Thus, the perimeter of MM identified by computer analysis is in many cases reduced.
in comparison with nevi and the area stays almost the same. This may explain the differences of perimeter/area ratio between MM and melanocytic nevi, especially those observed in cases with pigment network at the periphery (figs 2 and 3). The perimeter/area ratio can also be influenced by the overall shape of the lesion; however, the arrangement of the border seems to play a more important role.

The overall shape and colour asymmetry was more pronounced in MM than in benign nevi. We view the asymmetry of colours and structures as more important than the overall shape asymmetry. It has been already pointed out by the others that the clinical judgement of asymmetry is often based on an internal distribution of pigmentation also in overall shape symmetric lesions. The relative insignificance of the overall shape of examined lesions is also supported by the lack of importance of the compactness index in our study.

In summary, we found differences in arrangement of the border, size of the lesion (area, perimeter, maximal diameter) and asymmetry of shape or colour distribution by the comparison of predominantly thin MM, and atypical and common melanocytic nevi. Several parameters were verified as statistically significant even when comparing only clinically difficult cases. The perimeter/area ratio was recognized as the most important criterion in our study. By using perimeter/area ratio and asymmetry along A1 axis the statistical formula for calculation of the probability of malignancy of every analysed lesion can be constructed.

It is important to also comment on the number of excluded cases. It is always necessary to control the computer analysis carefully, particularly the basic process of segmentation of the digital image. If the border of the analysed lesion is not correctly detected, all results of computer analysis are worthless. This was the case for 45 of the 305 lesions in our study. We consider it important to
include these unsuccessful cases in the text and to warn of the necessity of boundary detection control to prevent falsifying the results. This analysis failure is common in partially hypopigmented nevi and melanomas with regression at the periphery. Defects in boundary detection are common in about 10–15% of clinically difficult cases.

Digital dermatoscopy is established as a helpful second-step procedure for the management of selected cases of pigmented skin lesions. The main advantage of the method is the digitalization of dermatoscopy images. This enables objective analysis of single cases and high-quality follow-up of patients with multiple melanocytic nevi or atypical lesions.

Digital dermatoscopy also facilitates the comparison of different lesions, medical consultations, presentation of interesting cases, and continual education. The role of digital computer analysis and computer-assisted diagnosis in daily practice is still controversial. Computer analysis offers objective and comparable results. Some parameters are more important than others in distinguishing MM from melanocytic nevi. The accuracy of differential diagnosis increases when several parameters are combined. However, as Ackerman says, the criteria identified as significant for atypical melanocytic nevi are the very same as those employed all over the world for the diagnosis of melanoma (ABCD criteria).

Atypical nevi and thin MM can overlap in sporadic cases, as no distinct border exists. All results of digital computer analysis must always be correlated with the patient's history, clinical nature of the lesion and conventional dermatoscopy assessment. Despite technical advances, the dermatologist is ultimately responsible for the quality of diagnosis of pigmented skin lesions. The definitive outcome is how to manage the patient – excision and histology is necessary, follow-up is useful or the lesion is unambiguously benign. The computers should supplement, not replace the dermatologist in future.

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References


