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# Comparison of Dermatoscopic ABCD Rule and Risk Stratification in the Diagnosis of Malignant Melanoma

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**For didactic and documentation purposes the dermatoscopic ABCD rule and the dermatoscopic risk stratification have been proposed. The aim of this investigation was to compare the ability of the 2 methods to separate patients with cutaneous malignant melanoma from individuals with other pigmented skin lesions. Three dermatologists, experienced users of dermatoscopy, assessed macroscopic clinical and dermatoscopic slides from 258 patients referred to the skin cancer outpatient clinic by the ABCD rule and risk stratification methods. Diagnostic performance of the 2 methods was compared by receiver operating characteristics curve analysis. When all pigmented skin lesions were compared, there was a trend for the observers to perform better using risk stratification. When only lesions with a well-defined pigment network were included, the diagnostic performance of the risk stratification method was superior to the dermatoscopic ABCD rule (areas under the receiver operating characteristics curve median 0.93 vs. 0.80, $p < 0.004$) for all observers. The agreement between the 2 methods was moderate to substantial (kappa coefficient 0.53–0.62). More melanomas were identified when the rules were combined. The dermatoscopic ABCD rule has been accepted as a standard for identifying melanomas with the dermatoscope, but should be considered secondary to pigment network analysis.** ***Key words: dermatoscopy; melanoma; receiver operating characteristics; dermatoscopic ABCD; risk stratification.***

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Clinical case finding of cutaneous malignant melanoma has improved with the advance of dermatoscopy (episcopy, dermoscopy, epiluminiscence microscopy). The dermatoscope is a handheld scope, similar in size to an ophthalmoscope that allows inspection of pigmented skin lesions at an approximately 10× magnification. A strategy for interpretation of the dermatoscopic findings is necessary. Proper use of dermatoscopy requires training and expertise (1, 2). Dermatoscopic criteria have been studied extensively (3, 4), which has led to rules for identification of pigmented skin lesion being suspicious of malignancy. Two methods have gained interest for recognition of cutaneous malignant melanoma (CMM): the dermatoscopic ABCD rule by Stolz et al. (5–7) and the dermatoscopic risk stratification method (8, 9).

The ABCD rule acknowledges the fact that no single element of dermatoscopy is 100% indicative of CMM. For this reason it was proposed that a total dermatoscopy score (TDS) should be calculated from the identification of individual dermatoscopic findings (Table I). The dermatoscopic ABCD rule has been re-evaluated (10–12). We have found, that simple pattern recognition performed by trained observers was superior to the ABCD rule (10), indicating that even the presence of a single high-risk feature may rank lesions as no, low-, medium- or high-risk elements. Kenet et al. suggested risk stratification based on disturbances in the pigment network of pigmented skin lesions (9). Some pigmented skin lesions show unambiguously benign features and some malignant melanomas show highly indicative malignant features. The purpose of the present investigation was to determine which of the techniques was superior in identifying CMMs.

## MATERIAL AND METHODS

Three senior dermatologists with more than 5 years daily experience in clinical use of dermatoscopy and familiar with the dermatoscopic ABCD rule (7) and the risk stratification method by Kenet & Fitzpatrick. (8) evaluated photographic clinical and dermatoscopic slides of pigmented skin lesions from 258 patients. From 1995 to 1999 clinical photographs and dermatophotographs were obtained from patients consecutively referred to the skin cancer outpatient clinic. Only patients having taken clinical photographs, dermatophotographs and a subsequent excision biopsy were included. The Heine S-10 Dermaphot lens and a modified Olympus camera (Heine Optotechnich) was used. The slides were projected to an 80 × 120 cm screen in a darkened room. Based on time studies in the outpatient clinic, each patient case was shown for approximately 3 min, which the observers accepted as sufficient time. Additional time was allowed if any needed it. The observers performed the assessments independently of each other using entry forms for the elements of the dermatoscopic ABCD rule (Table I) and the pigment network features according to the risk

Table I. *Dermatoscopic ABCD rule*

| | Weighting factor | Possible scores | Min.–max. |
|---|---|---|---|
| Asymmetry | 1.3 | 0–2 | 0–2.6 |
| Border | 0.1 | 0–8 | 0–0.8 |
| Colour | 0.5 | 1–6 | 0.5–3 |
| Light brown | | | |
| Dark brown | | | |
| Red | | | |
| White | | | |
| Bluish | | | |
| Black | | | |
| Differential structures | 0.5 | 0–5 | 0–2.5 |
| Dots | | | |
| Globules | | | |
| Network | | | |
| Streaming | | | |
| Homogenous areas | | | |
| Total dermatoscopy score | | | 0.5–8.9 |



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Table II. *Risk stratification*

| Stratum | Dermatoscopic findings |
|---|---|
| 1: Probable CMM | Pseudopods |
| | Radial streaming |
| | Heterogeneity of PN with thick dark extensions at the edge |
| | Blue-grey areas, white scarlike areas and presence of PN |
| 2: Possible CMM | Marked irregular network with irregular pigment confluence |
| | Eccentricity of PN with darkest regions near edge |
| 3: Atypical naevus | Patchy PN ± pink areas |
| 4: Benign naevus | Brown PN that fades at periphery |
| | Regular globular pattern |
| 5: Other pigmented skin lesions | Basal cell carcinoma, seborrhoeic keratosis, histiocytoma, angioma, blue naevus, pigmented Spitz naevus |

CMM: cutaneous malignant melanoma; PN: pigment network. One dermatoscopic finding is sufficient to determine the stratum.

stratification (Table II). All skin lesions had been excised and sent for histopathological examination. In addition to HE-staining, HMB-45 (13, 14) and S-100 immunostaining were performed to identify melanocytic lesions. Breslow depth and Clark level were determined. All cases were assessed by an experienced dermatopathologist. The histopathological diagnoses were used as the final diagnosis for calculation of diagnostic probabilities.

Data were entered into an electronic database, which was programmed to calculate the total dermatoscopy score as described by Stolz et al. (6), i.e. TDS = 1.3 × Asymmetry + 0.1 × Border + 0.5 × Colours + 0.5 × Differential structures (Table I).

Receiver operating characteristics (ROC) curves were plotted to compare the performance of the dermatoscopic ABCD and the dermatoscopic risk stratification method, respectively. ROC curves are constructed by plotting sensitivity against (1−specificity) for all possible cut-off points of the criterion. Three categories (non-melanoma, possible and probable melanoma) was devised for allocating patients as both systems devised these categories. Distribution-free methods were used for calculating areas under the ROC curves. Data from the 2 methods were paired as they were derived from the same sample of patients and significance testing of areas was adjusted for the rank correlation between ratings (15). The computer software "ROC analyzer v.5" was used (16). The area under ROC curves is proportional to the probability that a diseased individual will score higher than a disease-free individual (17) (Fig. 1). An area of 0.5 indicates a useless test and an area of 1 a perfect test.

In addition to the non-parametric analysis of diagnostic performances of the singular observers using the 2 methods, maximum likelihood estimates of the areas were used in a 3-way mixed factor design ANOVA as described by Dorfman, Berbaum and Metz (DBM) (18). The DBM allows analysis of the main effects: method (risk stratification vs. ABCD), observers and patient cases and the 2-factor interaction terms: method-observer interaction, method-patient and observer-patient interaction and finally a 3-factor interaction term and residual variance. The computer software "LABMRMC" (19) was used for this analysis.

Agreement between the 2 methods was analysed using Cohen's kappa for the categories: probable melanoma (stratum 1 in the risk stratification method and TDS > 5.45 in the dermatoscopic ABCD rule) + possible melanoma (stratum 2 and TDS between 4.75 and 5.45) vs. non-melanoma (stratum 3–5 and TDS < 4.75). Landis & Koch suggested a ranking of the kappa coefficient: 0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial and 0.81–1 almost perfect agreement (20).

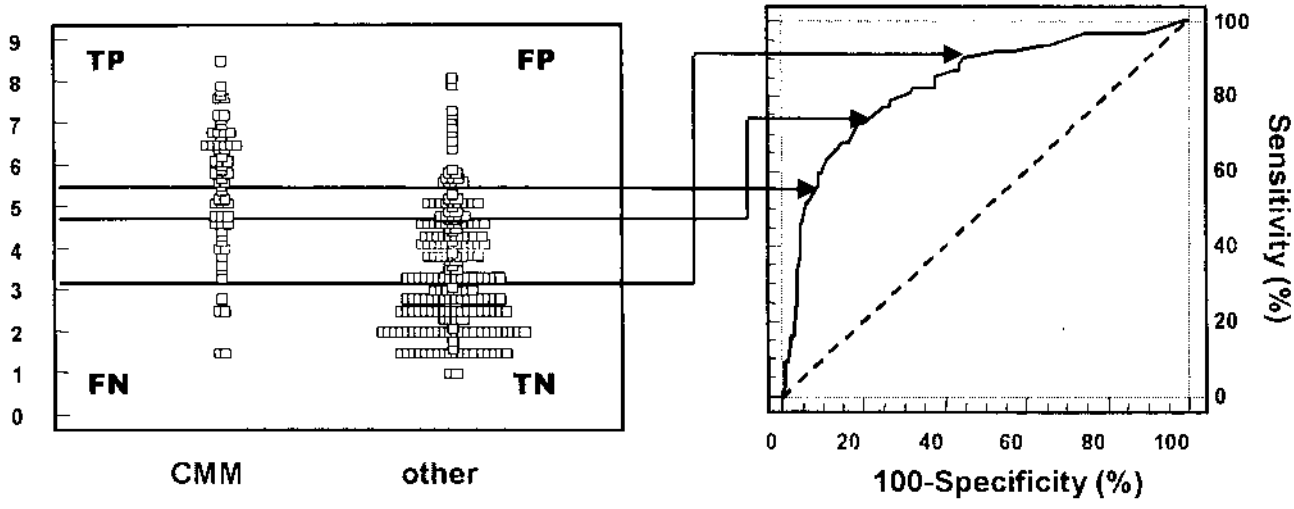


*Fig. 1.* Relationship between the dot-plot and the receiver operating characteristics (ROC) curve for total dermatoscope score (TDS). In the dot-plot individual observations for histologically proven malignant melanomas and non-melanoma pigmented skin lesions are plotted. Combinations of sensitivity and specificity for TDS = 5.45, 4.75 and 3.2 as cut-off points are arrowed to the ROC plot. In the dot-plot true positives (TP) are to the upper left of the cut-off criterion value, false positives (FP) to the upper right, false negatives (FN) to the lower left and true negatives (TN) to the lower right. The fraction (TP + TN)/(TP + TN + FP + FN) is related to the area under the ROC curve.

Table III. *Areas under the receiver operating characteristics (ROC) curves for the dermatoscopic risk stratification (RS) and the dermatoscopic ABCD rule for the entire set of pigmented skin lesions assessed by observers 1–3. Column 5 lists areas under the ROC curves when cutaneous malignant melanoma by at least one of the methods is considered the cut-off point. Last 3 columns: areas under ROC curves for lesions with a pigment network (PN)*

| Observer | All lesions | | | | PN | | |
|---|---|---|---|---|---|---|---|
| | RS | ABCD | *p*-value | Combined | RS | ABCD | *p*-value |
| 1 | 0.88 | 0.82 | <0.05* | 0.90 | 0.94 | 0.82 | 0.0037 |
| 2 | 0.88 | 0.80 | 0.02* | 0.87 | 0.93 | 0.80 | 0.0019 |
| 3 | 0.86 | 0.80 | 0.09 ns | 0.91 | 0.93 | 0.78 | 0.0001 |

## RESULTS

One hundred and thirty-five (52.3%) lesions were pigmented naevi, 64 (24.8%) were CMM, 25 (9.8%) pigmented basal cell carcinomas, 11 (4%) blue naevi, 14 (5.5%) seborrhoeic keratoses, 3 (1.2%) were dysplastic naevi and 1 pigmented Spitz naevus. The remaining were angioma, haemorraghia, papilloma and dermatofibroma.

The median (non-parametric) area under the ROC curve was 0.88 with the risk stratification method and 0.80 with the ABCD rule (Table III). The separation of CMM from other lesions was significantly better for observers 1 and 2 using the risk stratification method. The two methods combined (i.e. a positive CMM diagnosis by at least 1 of the methods) performed better than the dermatoscopic ABCD rule for all observers ($p<0.05$) and for observer 3 also better than the risk stratification method alone ($p=0.05$) (Table III). When only lesions with a pigment network were included, the areas under the ROC curves were significantly increased to a median of 0.93 with the risk stratification. Areas were unchanged with the ABCD rule and significantly lower than the corresponding risk stratification area ($p<0.004$) for all observers (Table III).

When only histologically proven melanocytic lesions and melanomas were included, risk stratification ROC areas were higher than ABCD ROC areas for observers 1 and 2 (0.92 vs. 0.83, $p=0.04$ and 0.90 vs. 0.81, $p<0.01$) and a similar tendency was found for observer 3 (0.87 vs. 0.81, $p=0.08$).

ROC curves are characterized in Table IV by the combinations of sensitivity and specificity for the cut-off points of possible and probable CMM. Specificity was similar for the 2 methods, but risk stratification was more sensitive yielding the larger areas under the ROC curves.

Using the DBM method, the jack-knife maximum likelihood estimates of areas for the risk stratification and ABCD rule was 0.96 and 0.91, respectively. This difference was not significant (Table V). The 95% confidence interval for the difference between areas was −0.03 to 0.13, meaning that at a specificity chosen at random, we would be 95% confident that sensitivity would favour the ABCD rule less than 3% and favour risk stratification less than 13%. Observer effect was not significant ($p=0.07$). Patient case effect was significant. The 2-factor interaction term: method-observer was non-significant with $p=0.09$. The difference between maximum likelihood estimates of areas under ROC curves for risk stratification and ABCD was significant at the 5% level for observers 1 and 2, whereas no difference was seen for observer 3.

The observed agreement between the 2 methods (using a TDS of 4.75 as cut-off point in the dermatoscopic ABCD rule and stratum 2 as cut off for the risk stratification—both including possible melanomas) in diagnosing cutaneous malignant melanoma ranged from 83% to 87%. The kappa coefficients ranged from 0.53 to 0.62 corresponding to moderate to substantial agreement. The bias adjusted kappa coefficients (21) were almost identical to non-adjusted values. Thirteen to 17% of assessments were disconcordant. In the disconcordance caused by a positive CMM diagnosis by the ABCD rule and a negative melanoma diagnosis by the risk stratification observer 1 had 4 superficially spreading CMM and 1 lentigo maligna, observer 2 had 3 CMM and observer 3 had 8 CMM. Non-melanomas classified as CMM by the ABCD rule, but not by the risk stratification method were compound naevi and pigmented basal cell carcinomas.

In the disconcordance caused by negative CMM diagnosis by the ABCD rule and a CMM diagnosis by the risk stratification method observer 1 had 10 CMM, observer 2 had

Table IV. *Combinations of sensitivity and specificity for cut-off values of possible (P) and probable (M) melanomas*

| Observer | | Risk-stratum | | ABCD | |
|---|---|---|---|---|---|
| | | Sensitivity | Specificity | Sensitivity | Specificity |
| 1 | P | 0.89 | 0.87 | 0.74 | 0.88 |
| | M | 0.80 | 0.95 | 0.46 | 0.94 |
| 2 | P | 0.89 | 0.80 | 0.74 | 0.81 |
| | M | 0.84 | 0.90 | 0.59 | 0.91 |
| 3 | P | 0.79 | 0.92 | 0.64 | 0.95 |
| | M | 0.75 | 0.94 | 0.30 | 0.99 |

Table V. *Dorfman, Berbaum and Metz ANOVA for multiple reader, multiple cases receiver operating characteristics comparison*

| Source | Df | MSq | Probability |
|---|---|---|---|
| Method | 1 | 1.0546 | 0.16 |
| Cases | 264 | 0.2739 | <0.01 |
| Observer | 2 | 0.3718 | 0.07 |
| Method-case | 264 | 0.1322 | <0.01 |
| Method-observer | 2 | 0.2377 | 0.09 |
| Observer-case | 528 | 0.1379 | * |
| Method-observer-case | 528 | 0.0966 | |

Df: degrees of freedom, Msq: mean squares.
*Three-factor interaction (method-observer-case) source of variance may not be negligible. Therefore the 2-factor interaction: observer-case is not tested in this ANOVA

9 CMM and observer 3 had 15 CMM. Non-CMM classified as melanomas by risk stratification but not by ABCD rule were blue naevi, seborrhoeic keratoses and a single case of pigmented Spitz naevus. Kappa statistics for the 3-level ranking of non-melanoma, possible and probable melanoma showed values identical to those for 2-ranks (not melanoma vs. possible + probable melanoma).

## DISCUSSION

The aim of clinical and paraclinical tests is to separate the diseased from the non-diseased population. When comparing the performance of 2 diagnostic test systems sensitivity, specificity, false positive and false negative rates are pivotal. ROC analysis is an accepted way of summing up these characteristics. The area under a ROC curve signifies the probability of correctly ranking diseased and not diseased individuals.

A random patient selected from a diseased group will have a higher test value than a person from a disease-free population with a frequency (%) determined by the area under the ROC curve. Both risk stratification method and dermatoscopic ABCD rule resulted in areas under the ROC curves between 80% and 90% demonstrating competent separation of CMM and non-CMM, i.e. pigmented skin lesions of other aetiologies. The separation is not perfect. Some CMM scored lower than certain non-CMM lesions and vice-versa. We found a better separation using risk stratification than using the ABCD rule when only lesions with a clear pigment network were included. This indicates that pigment network analysis is an integral part of a dermatoscopic examination. In the ABCD rule presence of radial streaming or cut-off border only score insignificantly by themselves despite the fact that radial streaming or pseudopods are certain indicators of CMM. The total dermatoscopy score was developed employing logistic regression analysis and multivariate modelling. The statistical methods imply that all possible factors in a test system must be taken into consideration at the same time. When using the ABCD rule an observer must evaluate 21 different factors (2 asymmetry, 8 border, 6 colours and 5 differential structures) in order to assess the CMM risk. With risk stratification a single CMM indicator is sufficient. It has been stated that no single dermatoscopic element in itself is sufficient to elicit a diagnosis of CMM. Dermatoscopic images have a histological counterpart and are projections of vertical sections to a horizontal view. Therefore a histologically malignant growth pattern should be recognizable dermatoscopically.

The diagnostic process for trained physicians is deductive, whereas the diagnostic process for untrained clinicians is inductive. The deductive process is initiated by a diagnostic hypothesis based on pattern recognition and subsequently selection of appropriate test to confirm or reject the hypothesis. The inductive diagnostic process is set off by the gathering of symptoms, signs and paraclinical tests and based on this establishing a diagnostic hypothesis. Risk stratification represents the deductive and the ABCD rule the inductive process. Previously we have found that simple pattern recognition of dermatoscopic slides yield higher diagnostic performance than the ABCD rule and that this effect was especially prominent for expert observers (10). The present study demonstrates that pigment network analysis improves the separation of CMM from other pigmented skin lesions. While the ABCD rule considers all variables simultaneously, the risk stratification reflects a simple clinical diagnostic process because it looks for and provides positive signs (e.g. radial streaming) and negative signs that rules out the diagnosis (brown network that fades towards the edge). Dermatoscopic examinations are placed between the clinical and histopathological examination in the logical succession of test to achieve maximum information yield. For this reason focus should be placed on a high sensitivity as histopathology serves as a highly specific confirmatory test. The ABCD rule has been revisited in 2 recent papers. Feldman et al. (12) lowered the diagnostic cut-off point of the TDS to 4.2 to obtain a sensitivity of 0.88, but as a consequence a specificity of only 0.64. The diagnostic potential of the ABCD rule follows an underlying ROC curve and the scientific effort should be focused on developing additional diagnostic strategies for dermatoscopy to move the ROC curve to the upper left rather than moving along an existing curve. Argenziano et al. (11) compared the ABCD rule with an epiluminiscence microscopy 7-point checklist and demonstrated higher diagnostic performance with their checklist. The 7 points consist of 3 major criteria (atypical pigment network, grey-blue areas and atypical vascular pattern) and 4 minor criteria (streaks, blotches, irregular dots and globules and regression pattern). The presence of atypical pigment network, grey-blue areas and streaks is also part of the risk stratification method. They reported a sensitivity of 0.93 and specificity of 0.75 and maximum likelihood estimate of area under the ROC-curve of 0.98 for a pattern recognition method. This is similar to the maximum likelihood estimate areas for risk stratification in this study. The pinpoint vessels used in Argenziano et al.'s method is not (yet) incorporated in risk stratification because this finding is also seen in some seborrhoeic keratoses and benign papillomas.

Kittler et al. (22) annexed an E (enlargement and other morphological change) to the ABCD rule for patient reported morphological change of the skin element and found a significant higher area under the ROC curve. We have previously discussed a probabilistic view of dermatoscopy where a likelihood ratio (= sensitivity/(1 − specificty) is multiplied with the pre-test expectation in order to get a post-test probability of the lesion being a melanoma (2). Patient reported morphological changes is not a dermatoscopic finding, but rather a factor influencing pre-test expectation similar to patient records of previous or consanguine melanoma.

Bias adjusted kappa coefficients were identical to Cohen's kappa demonstrating that the ABCD rule does not systematically underestimate the melanoma risk as compared to risk stratification, but rather that the 2 methods focus on different aspects in the identification of CMM.

The DBM method allowed both extrapolation to the population of patients from which the sample of patients was drawn and extrapolation to the population of observers from which the three expert observers were drawn. The maximum likelihood estimates generally yielded higher areas under ROC curves than the non-parametric method, the latter being more conservative, especially with only 3 cut-off values.

Our data allows generalization of patient cases for each of the observers. Inference from the observer component of variance warrants caution as only 3 expert observers could be included and the risk of beta-error is 10% for detection of a

5% difference in ROC areas, whereas the risk of overlooking a 5% difference would be only 3% with 4 observers. Roe et al. (23) found that the empirical type I error rate did not stabilize with only 3 observers under varying condition and recommended 5 observers or more in multi-reader experiments. With these reservations, risk stratification and ABCD performed equally well. The interaction between cases and methods ($p = 0.001$) supports the assumption that risk stratification and dermatoscopic ABCD identifies different melanomas and that they supplement each other.

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