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Predictive power of irregular border shapes for malignant melanomas

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Background/purpose: The Irregularity Index is a measure of border irregularity from pigmented skin lesion images. The measure attempts to quantify the degree of irregularity of the structural indentations and protrusions along a lesion border. A carefully designed study has shown that the parameters derived from the Irregularity Index were highly correlated with expert dermatologists' notion of border shape. This paper investigates the predictive power of these parameters on a set of data with known histological diagnosis.

Methods: A set of 188 pigmented skin lesions (30 malignant melanomas and 158 benign lesions) was selected for the study. Their images were segmented and their border shapes were analysed by the Irregularity Index, producing four border irregularity parameters. The predictive power of these four parameters was estimated by a series of statistical tests.

Results: The mean values of the four border irregularity parameters were significantly different between the melanoma group and the benign lesion group. When using the four parameters to predict its disease status, the leave-one-out classification rate was 82.4%, and the area under the receiver operating characteristic curve was 0.77. A malignant melanoma was 8.9 times more likely to have an irregular border than a benign lesion.

Conclusion: This study confirmed that border irregularity is an important clinical feature for the diagnosis of malignant melanoma. It also indicates that the computer-derived measures based on the Irregularity Index capture to certain extent the kind of irregularity which is exhibited by melanomas.

Key words: border irregularity – computer-aided diagnosis – Irregularity Index – malignant melanoma – pigmented skin lesion – shape

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BORDER IRREGULARITY is an important clinical feature in the diagnosis of malignant melanoma (1–3). Benign nevi usually have round and oval shaped borders, while abnormal nevi tend to have irregularly shaped borders with protrusions and indentations. In spite of the fact that the border shape alone cannot provide a definite diagnosis for melanomas, an irregular border may indicate abnormal growth, with the spread of melanocytes in various directions, regression of invasion and/or genetic instability of the lesion. Therefore, border irregularity has been included in the well-known self-screening schemes such as ABCD and the Seven Point Checklist, which have been advocated by many dermatologists (4, 5).

Quantifying border irregularity in a clinically meaningful way is a non-trivial task (6). Often the border shape is estimated by simple means, for example a mathematical measure such as the compactness index (7–11) or a statistical measure such as the fractal dimension (6, 12–15). However, these measures are sensitive to noise, fail to recognize structural protrusions and indentations along the border, and correlate poorly to the expert dermatologists' notion of border irregularity (6, 16).

A recently developed new measure, called the Irregularity Index, overcomes some of the problems of the earlier measures in that it is sensitive to structural protrusions and indentations and is strongly correlated (correlation coefficient = 0.88) with expert dermatologists' evaluation of irregularity (17). These properties of the Irregularity Index have been shown in a carefully designed study, however the number of lesions tested was

relatively small. The prime objective of the study described in this paper was to investigate the predictive power of the Irregularity Index as a melanoma indicator on a much larger data set. By using a different method of image acquisition and a different method of boundary extraction, this study was also testing the robustness of the Irregularity Index.

Materials and Methods

Data set

The data set used for this study consisted of 188 pigmented skin lesion images selected randomly from the image database of the University of Birmingham. The skin lesions in the database were captured using a SIAscope, a Spectrophotometric Intracutaneous Analysis skin imaging device (18), manufactured by Astron Clinica, Cambridge, United Kingdom. A SIAscope produces a number of narrow-band images, ranging from 400 to 1000 nm. The imaging area is 24×24 mm with the lesion located at the centre. The image resolution is 566×768 pixels. After the imaging session, the pigmented skin lesion was excised and diagnosed by an expert histopathologist. Out of the 188 lesions, 30 were diagnosed as malignant melanomas and the remaining 158 were deemed to be benign.

Segmenting the lesion

Prior to shape analysis, the boundary of a lesion must be determined from its image. Images corresponding to the blue part of the spectrum were used for this purpose. In this range of wavelengths both skin pigments, the melanin and the haemoglobin, absorb most strongly, and structural collagen reflects relatively high levels of incident light through scatter. This combination of factors results in the best contrast achieved between the lesion and the surrounding skin simultaneously both for melanocytic lesions and for haemangiomas (which may be confused with melanomas).

The boundary extraction was carried out by a two-step algorithm developed by Claridge and Orun (19) and summarized here. First the body of the lesion is located by a histogram-based 'fusion' method (20) and a tentative boundary is determined. The boundary is further refined in a second step by using a 'profile modelling method'. A sigmoid function corresponding to the edge profile p and defined by

$$p(r, A, T, s) = \frac{A}{1 + s^{(r-T)}} \tag{1}$$

where r is the radial distance from the lesion centre, A is the amplitude, s is the edge sharpness and T is the location of the edge midpoint, is taken as an ideal representation of the lesion brightness profile. A set of lesion profiles, normal to the tentative boundary obtained above, is extracted from the lesion image. Each profile is then fitted with an optimal sigmoid using an iterative least-squares technique. The parameter T in Eq. (1) above corresponds to the midpoint of the sigmoid and thus the 'zero crossing' location on the lesion edge profile. This midpoint location is taken to lie on the lesion boundary. The coordinates collected from all the profiles form the border outline for the lesion. Fig. 1 shows two examples of lesion profiles overlaid with the optimally fitted sigmoid functions. Fig. 2 shows an example of a lesion border derived using the profile fitting method.

Measuring border irregularity

A quantitative measure of border irregularity is derived from the lesion outline represented as a

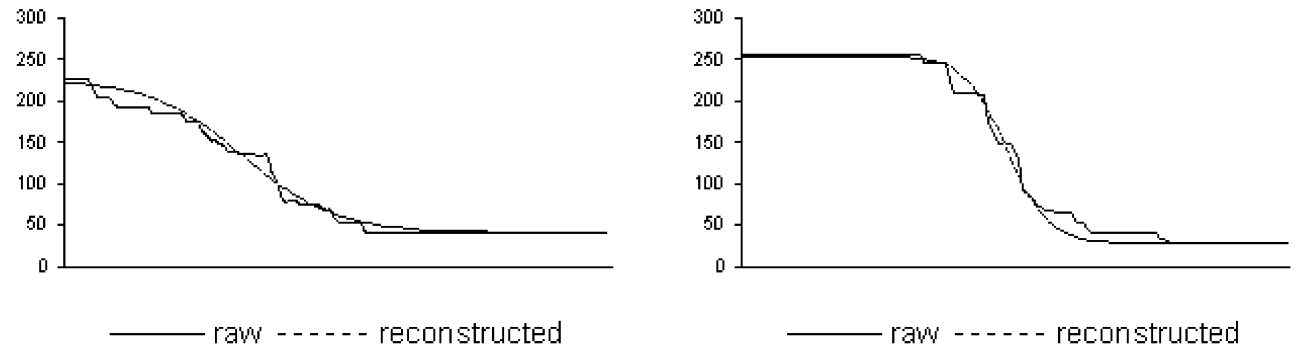

Fig. 1. Examples of two lesion profiles together with their reconstructed sigmoid models.

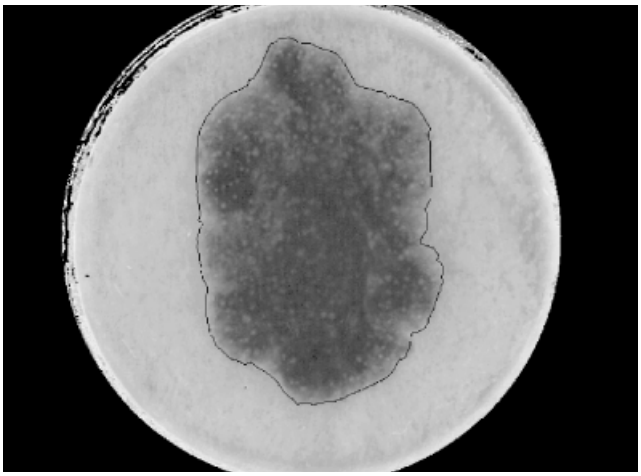

Fig. 2. An example of a pigmented skin lesion with its border outlined in black.

set of Cartesian coordinates. The chosen measure is the Irregularity Index, which has been designed to capture the structural indentations and protrusions along the border outline. The details of deriving the Irregularity Index have been described fully elsewhere (17); only a brief summary is presented here.

As illustrated in Fig. 3, the border can be partitioned into a set of overlapping indentation and protrusion segments based on the curvature function of the outline. Since the objective is to examine the characteristics of the structural indentation and protrusion segments, a multi-scale method is pursued. To this end, the lesion border is iteratively smoothed by applying a series of Gaussian filters until all concavities are eliminated, and the transformed border became an oval shape. An example of this procedure is shown in Fig. 4. After each iteration, the border is partitioned into overlapping indentation and protrusion segments, which are matched and tracked across all smoothing scales and the segment at the coarsest scale is defined as the structural segment. The ten largest structural indentation and protrusion segments of the lesion shown in Fig. 4 are highlighted in Fig. 5.

For every structural indentation and protrusion segment, the area affected by the smoothing process is then determined by subtracting the original lesion outline from each of the smoothed-out shapes, as shown in Fig. 6. The Irregularity Index is defined as the area corresponding to the difference between the two outlines, computed as above, normalized by the size of the original lesion. It is taken to depict an aspect of the degree of irregularity of the corresponding

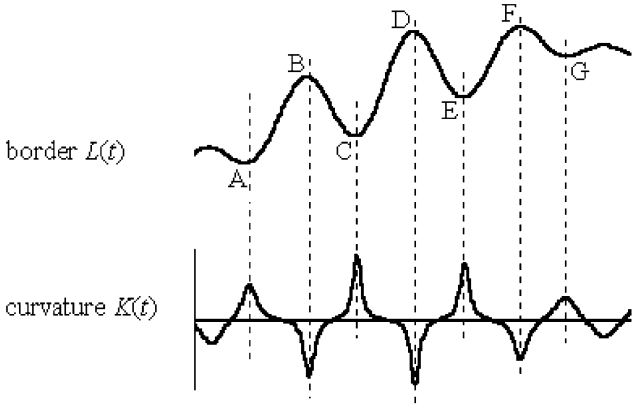

Fig. 3. Definition for indentation and protrusion segments. The border depicts a portion of an object border, where the interior of the object is below the border outline. The curvature shows the corresponding curvature function. The points A, C, E and G are the concave curvature extrema, while the points B, D and F are the convex curvature extrema. An indentation (protrusion) segment is defined as a curve segment that begins with a convex (concave) curvature extremum, is followed by a concave (convex) curvature extremum and ends with a convex (concave) curvature extremum. The border can be partitioned into a set of overlapping indentation and protrusion segments.

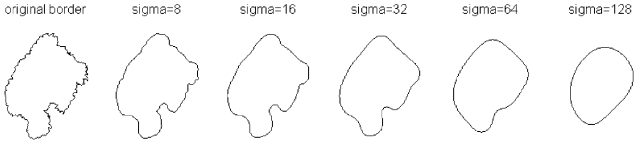

Fig. 4. Gaussian smoothing a lesion border until all concavities are eliminated.

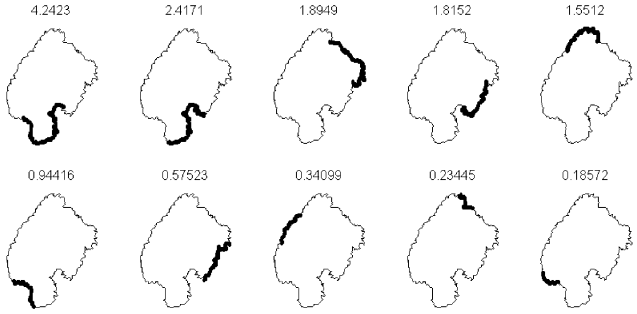

Fig. 5. The ten largest structural indentation and protrusion segments of the lesion border are highlighted. For each indentation/protrusion segment, an area-based index, called the Irregularity Index, is computed (see Fig. 6) and is shown at the top of the highlighted figure.

segment. Thus each lesion is characterized by a set of numerical measures derived from all structural indentations and protrusions along the border outline. The Irregularity Index for the ten largest segments shown in Fig. 5 is displayed at the top of the corresponding segment.

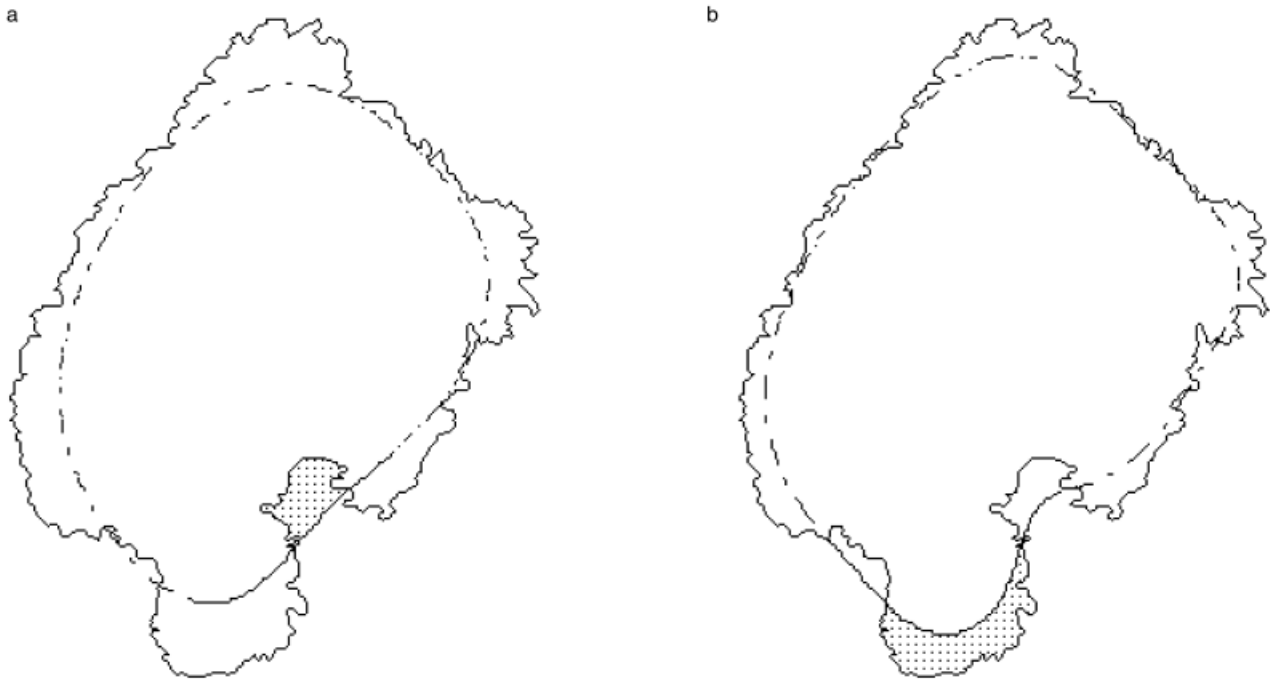

Fig. 6. (a) The shaded area is the filled-in area when the largest indentation segment of the lesion is smoothed out. (b) The shaded area is the removed area when the largest protrusion segment is smoothed out. These shaded areas are used to derive an area-based Irregularity Index for the corresponding indentation and protrusion segment.

Various statistical parameters could be produced from the set of Irregularity Indices of a lesion. The following four parameters have been found to be most relevant to lesion characterization (17).

- Indentation Irregularity Index (III): the sum of Irregularity Indices for all structural indentation segments;
- Protrusion Irregularity Index (PII): the sum of Irregularity Indices for all structural protrusion segments;
- Maximum Indentation Irregularity Index (MIII): the largest III's; and
- Maximum Protrusion Irregularity Index (MPII): the largest PII's.

The sum of III and PII was defined as the Overall Irregularity Index (OII) in an earlier user study (17), and it correlated highly with expert dermatologists' evaluation of the lesion border shape.

Statistical analysis

In order to evaluate the predictive power of the four border irregularity parameters, III, PII, MIII and MPII, statistical analysis was conducted including Student's *t*-test, linear discriminant analysis and receiver operating characteristic (ROC) analysis.

The mean and standard deviation of the four indices were compared for the melanoma group and the benign lesion group using the Student's *t*-test (21). It is generally accepted that a P value < 0.05 returned by the test indicates that the means are significantly different between the two groups.

A linear model (Eq. (2)) was built to classify the lesions into the predicted melanoma group and the benign group based solely on the four indices:

$$D = B_0 + B_1{*}\mathrm{III} + B_2{*}\mathrm{PII} + B_3{*}\mathrm{MIII} + B_4{*}\mathrm{MPII} \quad (2)$$

Discriminant analysis (22) was employed to determine the best coefficients B_i's which maximized the separation of the discriminant score D for the two groups. The resulting linear model was applied to predicate the malignancy of the lesions by thresholding the discriminant score D. A large score value inferred an irregular border and, hence, malignancy; on the other hand, a low score value implied a smooth border and a benign lesion. The rate of successful classification was estimated as the number of corrected classification over the total number of cases Eq. (3):

$$\text{Classification rate} = \frac{\text{number of true positives} + \text{number of true negatives}}{\text{number of all cases}} \quad (3)$$

A ROC analysis (23) was carried out on both, the indices III, PII, MIII and MPII, and the discriminant score D. The sensitivity and specificity of any diagnostic indicators can vary depending on the selection of the cut-off threshold for the diagnosis. The ROC analysis examines the sensitivity and specificity of all possible cut-off points. The area under the ROC curve is an additional, global, measure, which is commonly used to assess the overall predictive power of classification schemes. The areas greater than 0.9, 0.8, 0.7, 0.6 and 0.5 correspond to a test rated respectively as 'excellent', 'good', 'fair', 'poor' and 'worthless'.

Finally, the odds ratio (OR) (21) was computed to estimate the odds of a melanoma having an irregular border over the odds of a benign lesion having an irregular border. The lesion borders were divided into two groups, irregular and smooth border, respectively, according to the thresholded discriminant score D. The OR is then calculated by the following equation:

$$\text{OR} = \frac{\text{melanomas with irregular border} * \text{benign lesions with smooth border}}{\text{melanomas with smooth border} * \text{benign lesions with irregular border}} \quad (4)$$

An OR>1 implies that an increasing risk of linking melanomas with irregular borders.

The Student's t-test, discriminant analysis and ROC analysis were carried out by the statistical program SPSS for Windows, version 11.01 (SPSS Inc., Chicago, IL, USA).

Results

Student's t-test

Using the algorithm described in the section 'Segmenting the lesion', the 188 pigmented skin lesion images from Birmingham data set were segmented and verified. As an example, one of the images and its segmented border are shown in Fig. 2. The four border irregularity parameters, III, PII, MIII and MPII, were calculated for all the extracted borders. The means and standard deviations of these four parameters and their corresponding P values from the t-test are listed in Table 1. The melanomas have significantly larger means for all four parameters than the benign lesions. SDs for melanomas are also larger, but this indicator should be treated with caution because the sample size for the melanoma group is smaller than the benign lesion group.

Linear classifier

A linear model (Eq. (2)) is built using the border irregularity parameters, III, PII, MIII and MPII, as the independent variables of a discriminant analysis. All four variables were entered to the system simultaneously, and all contributed significantly to the classifier. The coefficients B_i's are tabulated in Table 2. The sorted discriminant score D is plotted against the lesion histology in Fig. 7. The mean values of the discriminant score D are significantly different between the melanoma group and the benign lesion group ($P = 0.000$). The mean D for the benign group is -0.20 with the 95% confidence interval (CI) = (-0.33, -0.07), and for the melanoma group the mean is 1.05 with the 95% CI = (0.43, 1.67). The classification rate of the model is estimated as 83.0% according to Eq. (3).

ROC analysis

The ROC analysis was performed on the border parameters and on the discriminant score. The areas under the ROC curves for the border parameters III, PII, MIII and MPII were 0.73, 0.71, 0.70 and 0.70, respectively. All these parameters had a

TABLE 1. Means, standard deviations and their P values by disease status for III, PII, MIII and MPII

	Mean		SD		
	Benign lesion	Melanoma	Benign lesion	Melanoma	*P*
III	1.14	2.39	1.13	2.20	0.000
PII	2.41	4.47	2.25	3.35	0.000
MIII	0.44	1.04	0.56	1.54	0.000
MPII	0.86	2.15	1.05	2.45	0.000

III, Indentation Irregularity Index; PII, Protrusion Irregularity Index; MII, Maximum Indentation Irregularity Index; MPII, Maximum Protrusion Irregularity Index.

TABLE 2. Discriminant analysis coefficients

	Coefficients for B_i's
B_0	-0.751
B_1	1.961
B_2	-0.797
B_3	-1.678
B_4	1.127

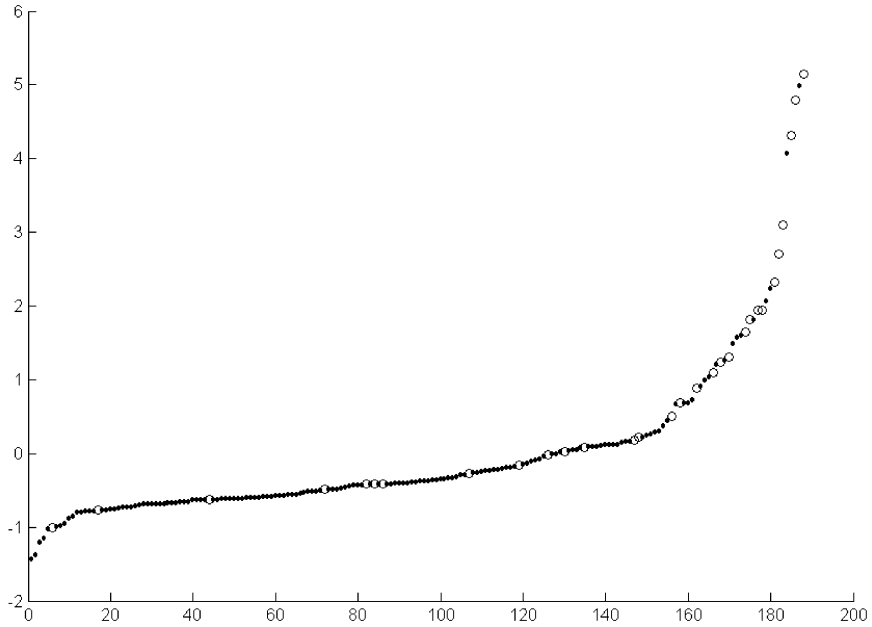

Fig. 7. The sorted discriminant scores are plotted sequentially along the x-axis. The benign cases are denoted by dots and the melanoma cases are denoted by open circles.

similar and moderate power in predicting malignancy, although the III outperformed the other parameters slightly. The area under the ROC curve for the discriminant score D was 0.77, which confirmed that the discriminant score improved the classification. The ROC curve of the discriminant score D is plotted in Fig. 8.

OR

The lesions were divided into the irregular and the smooth border groups by thresholding the discriminant score D at 0.4. On this basis the OR for a melanoma with irregular border was 8.9 with the 95% CI = (3.7, 21.2).

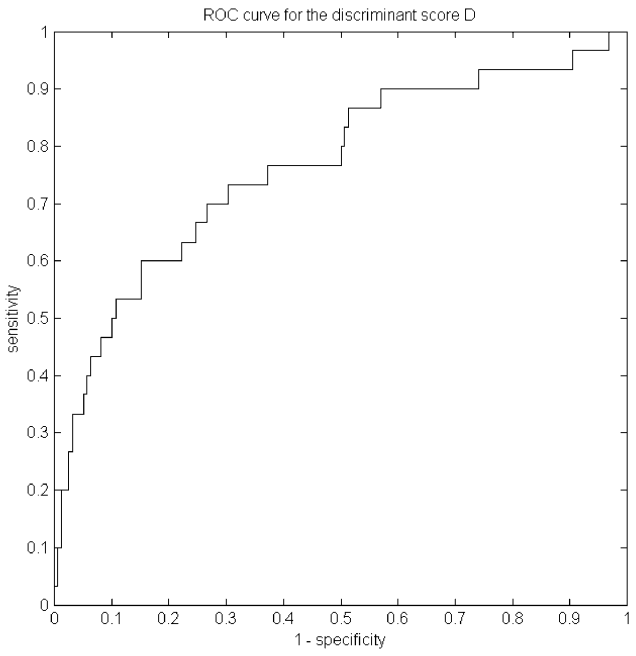

Fig. 8. The ROC curve for the discriminant score D.

Discussion

An earlier publication concerning the use of irregularity parameters has established that these indentation- and protrusion-based measures correspond well to the intuitive notion of irregularity used by experienced dermatologists in the assessment of pigmented skin lesions and diagnosis of melanoma (17). This study has investigated the predictive power of the irregularity parameters by a series of statistical analyses on a set of lesions with known histological diagnosis. The current study used a data set of 188 lesions, which is much larger than the original set of 40 lesions.

The Irregularity Index analysis described in section 'Measuring border irregularity' yields the following five border irregularity parameters: OII, III, PII, MIII and MPII. The OII was not included in the linear model (Eq. (2)) because it is the sum of the III and PII and the discriminant analysis does not allow the inclusion of such linear combinations as independent variables. The parameters III and PII provide an *overall* measure of indentations and protrusions, respectively. The other two parameters, MIII and MPII, provide a measure related to *the largest*

indentation/protrusion present in the lesion. Clinical experience suggests that both, border with many protrusions and indentation and border with one large protrusion or indentation may be indicative of melanoma. It should be noted that averaging indices, such as for example the average Irregularity Index, were excluded from any analysis because of the concern that such averaging measures do not really reflect the shape of the lesion border.

The results of the Student's *t*-test carried out on the four border irregularity parameters III, PII, MIII and MPII showed that each of these parameters could be used as a melanoma predictor (cf. Table 1). The subsequent discriminant analysis based on these parameters computed the coefficients yielding the best separation between the malignant and the benign groups. However, it is well-known that discriminant analysis may overestimate classification rates for the samples from which it derives the coefficients. Such an overestimation can be overcome by the *leave-one-out* analysis, where each lesion is left out in turn and the coefficients of the model Eq. (2) are computed. The left-out case is then classified by a model generated with the remaining n-1 cases. By freeing each case in turn from the coefficient computation, a less-biased classification rate can be determined. The leave-one-out analysis reduced the classification rate from 83.0% to 82.4%. It should be noted that the linear model of the discriminant analysis Eq. (2) is not intended as a general diagnostic system, since such a system should require other diagnostic features of the lesion related to its colour, size, pigmentation patterns, patient history and many others.

Although all four border irregularity parameters contributed significantly to the discriminant model, it is of interest to determine which parameter had the highest contribution. The unstandardized coefficients listed in Table 2 cannot be used in their original form since they represent the original independent variables, which have different orders of magnitude. Instead, the standardized coefficients reported by the SPSS program were used, where the coefficient with the largest absolute value corresponds to the variable with the greatest discriminating ability. The standardized coefficients were 2.654, -1.954, -1.330 and 1.538, for III, PII, MIII and MPII, respectively, and the coefficient for the III had the largest magnitude. Furthermore, the ROC analysis for the four border parameters revealed that the III had the largest area under the curve. The above evidenced suggest that indentations have higher predictive power than protrusions. This interesting observation may be related to the fact that indentations are often caused by regression, which is a strong indicator of malignancy.

It is well-known that the sensitivity and specificity of a score can vary substantially depending on the cut-off point. An increase in sensitivity may be achieved at the expense of specificity and vice versa. For example, when using the discriminant score D to predict malignancy, 100% of sensitivity for the discriminant score D could be achieved if the specificity is allowed to drop to 3.16%. Similarly, 100% specificity is achievable for sensitivity rate of 3.33%. Using the optimal threshold reported by the discriminant analysis resulted in sensitivity of 53.3% and specificity of 88.6%. These results, which correspond to a specific threshold, do not agree well with clinical decision-making reported by Menzies et al. (24), where an irregular edge is reported to be a highly sensitive (about 90%) but weakly specific (about 40%) predictor of melanoma. However, a different threshold at $D = -0.5$ applied to the same set of discriminant scores would yield sensitivity (90.0%) and specificity (43.0%) which are in agreement with clinical experience (see Fig. 7). The threshold selected through the discriminant analysis is likely to have arisen because in the data set analysed many melanomas appear to have relatively smooth borders. An explanation could be that the melanoma group comprised of more than half of early melanomas, which tend to have relatively small irregularities. The high specificity of the classification indicates that the majority of benign lesions have relatively smooth borders and only a few benign lesions may have irregular borders. Overall, these results confirm an expectation that melanoma classification cannot be based on the border shape alone. However, border irregularity is an important predictor. This is most clearly shown by the results of the OR analysis where melanomas are nine times more likely to have irregular borders than benign lesions.

Conclusions

This study analysed the predictive power of the indices generated from the Irregularity Index, a new measure of the degree of irregularity for the

structural indentations and protrusions along a lesion border. For a set of 188 pigmented skin lesions with known histological diagnosis, there is a 9-fold increase in the odds of melanomas with irregular borders than benign lesions. The study has also confirmed that melanoma classification cannot be based solely on the border shape, since border irregularity is only one possible manifestation of the disease. However, an 82.4% classification rate for the leave-one-out analysis and the area of 0.77 under the ROC curve indicates that the discriminant score based on the Irregularity Index represents a 'good', although not 'excellent' test for malignancy. Indentations were found to have marginally better discriminatory ability for malignancy than protrusions. Since the indices based on the Irregularity Index are highly correlated with the clinical notion of irregular border (17), this study may be taken as another confirmation that border irregularity is an important clinical feature. It also indicates that the computer-derived measures based on the Irregularity Index capture to certain extent the kind of irregularity, which is exhibited by melanomas. Work is underway to include the measures based on the Irregularity Index into a classifier incorporating other lesion features.

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