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A decision support system for the diagnosis of melanoma: A comparative approach

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ABSTRACT

Melanoma is the most deathful of all skin cancers and the number of cases grows every year. The extirpation in early phases implies a high degree of survival so it is fundamental to diagnose it as soon as possible. In this paper we present a clinical decision support system for melanoma diagnosis using as input an image set of the skin lesion to be diagnosed. The system analyses the image sequence to extract the affected area, determinates the characteristics which indicate the degree of damage and, according to them, it makes a decision. Several methods of classification are proposed: a multilayered perceptron, a Bayesian classifier and the algorithm of the *K* nearest neighbours. These methods work independently and also in combination making a collaborative decision support system. The classification rates obtained are around 87%.

1. Introduction

The incidence of melanoma skin cancer has been increasing over the past decades. Since the early 1970s, melanoma incidence has increased significantly, for example an average 4% every year in the United States. Currently, 132,000 melanoma skin cancers occur globally each year (World Health Organization, 2010).

Melanoma is the most deathful of all skin cancers. The main cause of melanoma is due to a long exposition to ultraviolet radiations, although skin type or other genetic factors can influence too. The most effective treatment is an immediate extirpation, but just when the melanoma had been detected in early phases (Geller, Swetter, Brooks, Demierre, & Yaroch, 2007). In other cases, if it is not diagnosed in time, the life expectancy is reduced up to less than one year. Therefore, it is fundamental to distinguish as soon as possible between benign lesions (as a simple spot or a mole) and melanomas. Dermatologists employ for their diagnosis several techniques which have been developed based on experience, among which it is emphasized to obtain the total dermatoscopy score based on the mnemonic ABCD (Stolz, Rieman, & Cognetta, 1994), the rule of 7 points (Argenziano et al., 1998) and the method of Menzies (Menzies, Ingvar, Crotty, & McCarthy, 1996). All these techniques allow identifying symptom of a malignant lesion based on the observation of a set of characteristics using dermoscopy images. Even so, in some cases it could be a hard task, the interpretation of these properties visually, and therefore, to make a right diagnosis.

We propose a clinical decision support system that classifies images with suspicious skin lesions in order to manage a referral list to the specialist. The patients whose images present a high probability of being a melanoma will be referred to the dermatologist as soon as possible. There are other clinical decision support systems implemented with this idea of managing a referral list; one example is the ERA (Early Referral Application), a system to support family doctors in identifying patients with suspected cancer that should be referred to a specialist in a short time period (Coiera, 2003). The system can also be used by a dermatologist as a second expert opinion to complement and compare his decision. It is important to bear in mind that the clinical diagnosis of melanoma depends on the dermatologist's experience (Kittler, Pehamberger, Wolf, & Binder, 2002) so a second opinion can be important for a dermatologist in a training period or at the beginning of the professional activity.

The system bases its automatic diagnosis in three phases: detection, description and classification of the lesion (Fig. 1). In the first phase a preprocessing of image is done which allows us to identify the affected area. Afterwards, in the description phase, the image to determinate the optimum set of characteristics which indicate the degree of malignant tissue is analysed. Finally, this characteristics vector is used as the input of an artificial entity that is able to offer a diagnosis of the lesion, classifying it as a melanoma or a benign lesion. The entities proposed here are the method of the *K* nearest neighbours, a parametric classifier based on the decision theory of Bayes, a multilayer perceptron and the combination of these three methods in a voting collaborative system.

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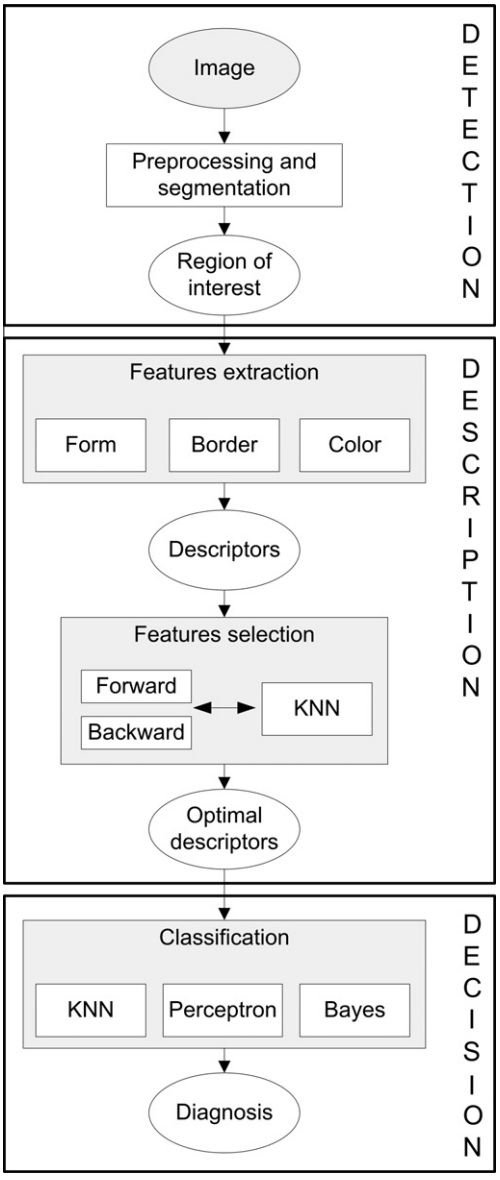

Fig. 1. Phases of the clinical decision support system to diagnose melanoma.

2. Related work

The importance of the topic is patent if we analyse the enormous quantity of researches related with the melanoma diagnosis using different ways to analyse the images automatically (Malene, Vestergaard, & Menzies, 2008). Sometimes, it is possible that software can recognize features when the eye cannot and therefore improve the diagnostic accuracy. In this section we will show some of these researches, related with the work we present.

Dermoscopy is a non-invasive examination technique based in the use of incident light and oil immersion to make possible the visual examination of subsurface structures of the skin. The rate of detection of melanoma using dermoscopy is higher than detection only with unaided observation (Kittler et al., 2002). In any case, the diagnostic accuracy of dermoscopy is also depending on the training of the dermatologist.

We can find several methods that use dermoscopy images. For example, the method presented in (Ganster et al., 2001) implements a segmentation of the affected area applying different types of algorithms (thresholding in the blue plane, searching 3D colour sets, etc.); afterwards they calculate a set of radiometric characteristics, and global and local parameters to describe the malignity of the lesion; finally, the more significant characteristics are selected using statistical methods. The work presented in (Schmid-Saugeon, Guillod, & Thiran, 2003) consists on a system for melanoma diagnosis taking into account border detection and quantification of asymmetry rate; its outline detector employs a technique based on clustering with fuzzy *C*-means algorithm and classification is based on a rate of symmetry quantification uniquely with a six dimensions vector. Other works, as the presented in (Zagrouba & Barhoumi, 2005), use the segmentation by pixel adding with a previous processing based on fuzzy sets; an attribute series is extracted from the detected area and processed by a neuronal network to distinguish between melanomas and benign lesions.

An interesting approach is the use of different techniques combined to improve the accuracy of the classification. For example, in (Sboner et al., 2001) the system introduced detects the lesion using a thresholding technique based on the red component and the saturated component; the system extracts a colorimetric and geometric characteristic set, with which a diagnosis is performed using a voting system, taking into account the produced results by different instances of the *K* nearest neighbours algorithm. In (Kreutz et al., 2001) a classification method for tissue lesions based on the use of artificial expert entities is proposed; a set of characteristics related to the lesion asymmetry, uniformity of outline and tissue, is determined and they will be employed for training a multi-agent classifier. This multi-agent is composed by a series of neural networks managed by a master entity that gives input vectors and generates a final diagnosis adjusted to the output of its different components.

A modern method for the assessment of melanoma is the lacunarity analysis (Gilmore, Hofmann-Wellenhof, Muir, & Soyer, 2009). Lacunarity is a measure used to characterize a property of fractals and quantifies aspects of patterns that exhibit changes in structure; lacunarity measure can reveal additional information regarding the geometric structure of melanocytic lesions and it is possible to distinguish melanoma from non-melanoma lesions with a 91% of sensibility and a 61% of specificity. The main problem of this algorithm is the low specificity; this means that the algorithm can diagnose a non-melanoma as a melanoma so it is not very useful to reduce the number of useless biopsies.

As we can appreciate, most of the researches related to an automatic melanoma diagnosis are based on techniques such as the algorithm of nearest *K* neighbours or neuronal networks, although there are other techniques that use lineal classifiers or image interpretation methods. Nevertheless, we have not found any work incorporating classifying methods based on statistics. In our work, we propose a classifier method based on Bayes theorem, and we compare his results with a multilayer perceptron and the algorithm of *K* nearest neighbours. Furthermore, very few works are found where different individual methods are used to constitute a voting system in which each input brings its decision with a determined weight. We also analyse a voting system combining the methods developed in the work.

3. Detection of the lesion

3.1. Preprocessing

In order to do a diagnosis, before the image processing, we must solve several important problems related to the image type which the system is dealing with. In the first place, captures of human tissues could present hair or pores, which may mislead the segmentation process. The immediate solution would be shaving the hair before imaging sessions, but it is a process that, apart from increasing costs and time for obtaining samples, it is uncomfortable for the patient and it is impractical in many cases. In these

cases we will apply the algorithm of hair deleting proposed in (Chen et al., 2005; Lee, Gallagher, Coldman, & McLean, 1997) called DullRazor. This method consists of three phases: hair identification applying an operation of closure over each of the colour segments, hair pixels replacing by around tissue pixels and a final image smoothing (Fig. 2).

On the other hand, all digital images present impulse noise, which we will mitigate applying a filter. We have chosen a media filter because it offers the suppression of the small pores that can be on the skin and reduces possible reflections and shines which could appear in a dermoscopic image, preserving region outlines. We have tried different filter sizes (3, 5, 7, 9 and 11) and the best results are obtained using a mask size 7.

3.2. Segmentation

Segmentation is the main phase in an application of automatic image processing: post-analysis depends on this for carrying out a correct diagnosis. The objective here is to split objects that constitute the scenario for obtaining the affected region of the image. Several applicable methods exist for this purpose; among them, we emphasize pixel segmentation, region segmentation and border detection (González & Woods, 2007). We will use thresholding, which is a technique based on a pixel segmentation. In particular, we will apply an adaptive threshold method, because the image set to segmentation is very heterogeneous, and to establish a global threshold for everyone would not be viable.

The developed technique tries to choose in each case, automatically, the threshold that will split the affected region from the rest of the image; we will apply the Otsu method (Petrou & Bosdogianni, 1999). This is a technique of adaptive thresholding with the aim of separating two classes, searching to maximize distance between both classes and to minimize areas formed by points associated to each class. The resulted image from preprocessing stage, converted to grey scales, will be the input for this algorithm; the output will produce a binary image with segmented regions at high level (white) and the rest of the image at low level (black). An opening operation (an erosion followed by a dilatation) and afterwards, a closing operation (a dilatation followed by an erosion) with structured elements of size 3, are applied with the objective of smoothing the outline of the region of interest from the resulted image. The algorithm of connected components labelling with 8-connectivity is applied to binary images after morphological transformations and the objective is to identify objects which have been extracted in the segmentation process. Once we have all objects labelled, we keep the ones with the biggest size, which will correspond with the affected area. Finally the extracted region could have holes due to the automatic thresholding, we will process the image with a hole filling algorithm. This calculates its negative, segments the image in binary form, identifies the background and fills the rest of the image with value 1 (high level).

4. Description of the affected region

4.1. Extraction of characteristics

In this first stage of the description phase, we obtain a series of numerical descriptors that represent the clinical signs of the malignant lesion extracted in the previous phase.

According to the conclusion in (Johr, 2002), the automatic extraction of characteristics that take into account the rule ABCD is computationally less expensive than the ones that take into account, for example, the one of 7 points or the Menzies method. Furthermore, the reliability in the clinical diagnosis is very high. For this reason, we will base our study on the stipulated by the mnemonic ABCD:

Asymmetry. The two halves of the malignant lesion are different, both colour and texture.
Border. The melanoma borders are usually irregular and diffused.
Colour. The colour in the malignant lesion varies among the different lesion areas, including cinnamon or brown colour shades, and also black, red, and even blue and white shades.
Diameter. The melanoma diameter is usually bigger than 6 mm.

Taking into account the rule ABCD, we will obtain a series of characteristics which will be classified into three main groups: descriptors of shape, of border and colour and texture. The diameter measure will be included in several descriptors obtained.

Among the characteristics related to the shape, we obtain the *modification ratio*, *the relation of aspect*, the *extension* and the *shape factor*, that are the irregularity measures of the lesion structure; the *anisotropy* indicates the homogeneity that is the growth of the region from the mass centre to the exterior in any direction; and the *symmetry* in relation to the main and secondary axis of the lesion expansion and the global shape.

In the border, we evaluate, on the one hand, how the transmission between the segmented region pigment and the surrounding skin is, obtaining the *medium* and its *sharpness variation.* On the other hand, we analyse the abruptness of the outline, determined by the values of *roundness, compactness, irregularity index* and *fracture dimension.*

Finally, if we focus on the colour and texture characteristics, we will obtain the basic measures related to the *components average* RGB and HSL. Moreover, we will determine other descriptors that indicate the variety of colours and its distribution in the segmented area. Among them, we have the result of the *clustering of the region*, the *entropy and its homogeneity of colour*, and the way in which *the colour is correlated with the geometry.*

The characteristics of the described values show uneven levels and unities, which can be a negative influence in the subsequent classification process. To solve it, we apply an objective scale be-

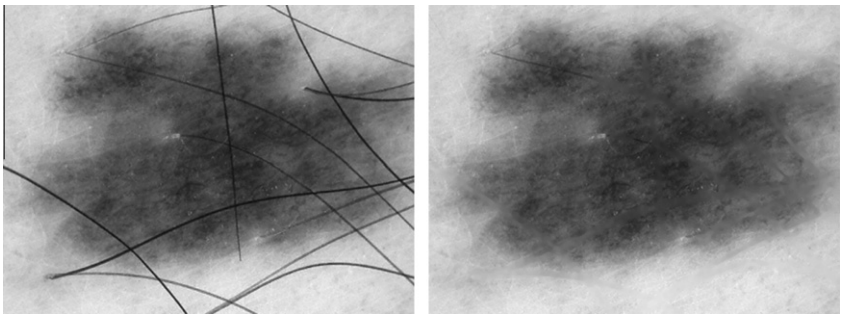

Fig. 2. Results of the algorithm of hair deleting.

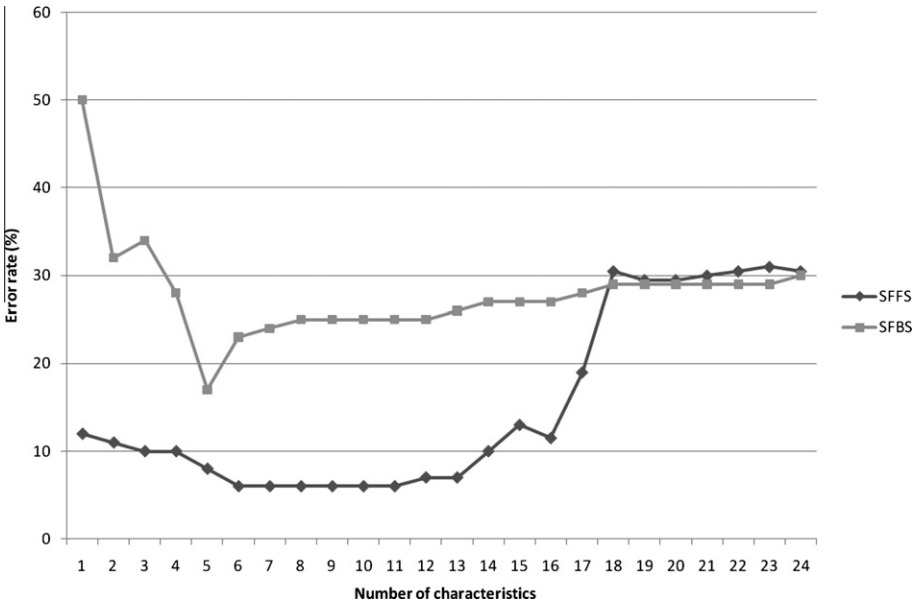

Fig. 3. Evolution of the classification error.

tween 1 and −1, obtaining the *z*-scores of the values of all the variables:

$$z_{ij} = \frac{x_{ij} - m_j}{\sigma_j} \quad (1)$$

where x_{ij} represents the *i*-ieth value of the characteristic *j*. m_j and σ_j represent the average and typical deviation, respectively.

4.2. Selection of characteristics

The objective of this phase is, from the set of 24 descriptors obtained in the previous stage, to determinate the minimum number m ($m < 24$) of the most relevant characteristics that can describe the malignant lesions as well as it would be done by the original set. This fact would reduce the dimension of the prototype of the lesion and, in consequence, the necessary computational time to process those, obtaining a higher output in the classification stage. Bearing in mind this goal, we use two algorithms of selection of characteristics: *Sequential Floating Forward Selection* (SFFS) and *Sequential Floating Backward Selection* (SFBS). These techniques require an objective function $F(y)$ to evaluate the classification error when using the descriptor set y.

As a function of evaluation, we use the algorithm of the *K* nearest neighbours (kNN). The reasons of the election are its high modularity (it allows us to incorporate/eliminate characteristics easily) and its low computational cost. To determinate the error rate in the classification we use the method of cross-validation, in which the total set of samples is randomly divided into separated subgroups of similar size. In each step, we request a classifier using one of the subgroups as test samples and the rest, as learning. This way, the resulting measures of classification are obtained from the average of all the answers of each of the constructions made from the classifier.

In the forward sequential algorithm, we start from an optimum subgroup of empty characteristics, which will be completed by each interaction with a characteristic that has a higher discriminatory power. The completion of the algorithm will be when, adding a new characteristic, the error percentage increases. The subgroup where the best benefits are obtained for the forward selection includes the following descriptors: shape factor, symmetry, extension and the averages of tone, saturation and lightness of the colour model HSL.

On the other hand, the backward sequential algorithm starts from the complete set of descriptors. In each interaction we extract the characteristic that offers the minimum error of classification when eliminating it. With it, the subgroup of characteristics generated by the smaller classification error for this algorithm is composed by sharpness variation, colour homogeneity of the lesion, average of the red and green colour component RGB and the average of colour luminescence HSL.

In Fig. 3 we can see the evolution of the error rate in the classification, according to the variation of the number of characteristics in the optimum subgroup for the forward and backward selection. The plateaus observed in the representation are due to the existing correlation among some variants.

As we can observe, the minimum classification error is located in the six descriptors for the SFFS algorithm of selection and in five for the SFBS algorithm. Although being higher, the set determined by the algorithm SFFS, we will use it as optimum, because the classification error produced is much lower than the SFBS with only five characteristics.

5. Classification

The last phase of the system is the one in charge of making the inferences about the extracted information in the previous phases in order to be able to produce a diagnostic about the input. In other words, the optimum features vector from the description phase will be employed to decide which type of lesion is closer to the input image: a benign lesion or a melanoma. In order to do so we will use four methods of classification. Three are individual: the algorithm of the *K* nearest neighbours, a Bayesian classifier and a multilayer perceptron; and the last one is a collaborative method that agglutinates the three previous ones using a system of votes.

Next, we give the details of the individual methods used:

a) The first individual method of classification is the algorithm of the *K* nearest neighbours, which is already used as validation function in the phase of selection of characteristic. This

diagnostic technique will classify a vector of characteristics of an image (x) by proximity of the patrons contained in the area K.

b) The second of the individual classifiers is based on the decision theory of Bayes. This theory says that a classification problem can be expressed in probabilistic terms; these terms are known or estimated [14]. In that way, if we have a patron x to classify, we will label it with class c_i, so that $P(c_i|x) > P(c_j|x)$ for all $j = 1 \dots C$ and $i \neq j$. Where $P(c_i|x)$ represents the a posteriori probability of the patron x belonging to the class c_i, and comes defined by the theory of Bayes:

$$P(c_i|x) = \frac{p(x|c_i) \cdot P(c_i)}{p(x)} \tag{2}$$

In practice, we do not know about a priori probabilities, $P(c_i)$, conditioned probabilities or functions of density of probability, $p(x|c_i)$. We can only have a vague idea of the "shape" of the functions and a well-classified sample set; that is why we must look for a way to determine these values.

If we suppose that we have $N = \{N_1, N_2, \dots, N_C\}$ prototypes belonging C classes, we can estimate the a priori probability by a simple counting as follows:

$$P(c_i) = \frac{|N_i|}{\sum_{j=1\dots C} |N_j|} \tag{3}$$

To estimate the probability density function we must make a supposition about its shape. The most tried is the Gaussian, due to, on the one hand, the function is completely specified by few parameters (the average μ_i and the matrix of curviness $\underline{\Sigma_i}$), and on the other hand, it is a reasonable approximation for the majority of the data taken from the nature. In this way we can define the density function as:

$$p(x|c_i) = \frac{1}{\sqrt{2\pi}\sigma_i} e^{-\frac{1}{2}\left(\frac{x-\mu_i}{\sigma_i}\right)^2} \tag{4}$$

We only had to estimate the values of μ_i and Σ_i. In order to do so we will suppose that there is not a correlation among the data characteristics, therefore the matrixes of curviness and the average of each class of the dominium will be calculated in the following way:

$$\begin{pmatrix} \sigma_{11}^2 & 0 & \cdots & 0 \\ 0 & \sigma_{22}^2 & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \cdots & \sigma_{mm}^2 \end{pmatrix} \tag{5}$$

$$\hat{\sigma}_{ii} = \frac{1}{N-1} \sum_{l=1}^{N} \left(x_i^l - \hat{\mu}_i\right)^2 \tag{6}$$

$$\hat{\mu}_i = \frac{1}{N} \sum_{l=1}^{N} x_i^l \tag{7}$$

where N is the number of class prototypes which the variant is being calculated about; m is the dimension and x^l is the l-ieth prototype of such class.

With all that we could calculate the value of $p(x|c_i)$ and we would have all the necessary variables to do the calculus of the a posterior probability, and then build the classifier that we are looking for. The learning process lies in determining the average values and curviness matrixes of each of the classes from the training set. When offering the diagnosis (D wining class) we will use the formula:

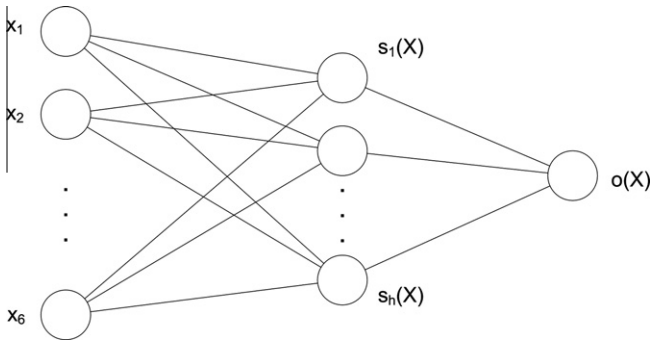

Fig. 4. Architecture of the proposed multilayer perceptron.

$$D = \text{argmax } c_j \in CP(c_j) \cdot \prod_i p(x_i|c_j) \tag{8}$$

a) Finally, the last of the three individual proposed methods is a multilayer perceptron, essentially due to its great adaptability, robustness, generalization capability and mistakes tolerance. We use an architecture with an input, a hidden and an output layer (Fig. 4).

The input layer will have a neuron per each characteristic of the optimum set of descriptors. The number of neurons of the hidden layer (H) will be determined in an experimental way in the following section. In each neuron we will apply the *sigmoidea* as a function of activation, $s_i(X)$. Finally, the output layer will present a unique neuron whose activation function, $o(X)$, will correspond to the application of a threshold. Once the architecture of the perceptron is defined, we apply the back-propagation algorithm, in order to adjust the weights that minimize the error originated when classifying the set of training patrons.

Taking these three methods as a whole we can define a vote system. Each of the individual methods of classification offers its decision about the input, as well as a reliability percentage about the diagnosis (c_i). These values are employed to determinate a global decision to all the individual entities, which will be offered by the collaborative system. If we consider M the number of entities that have diagnosed, the entrance as melanoma and B the ones that have diagnosed a benignant lesion, we can define the following value:

$$Sum_{global} = \sum_{j=1}^{M} c_j - \sum_{i=i}^{B} c_i \tag{9}$$

This way, if Sum_{global} is bigger than or equal to zero, the voting system diagnoses the input as melanoma and in any other case as benign lesion.

6. Experimentation and results

We have used, as input to the system, images acquired by means of dermoscopy technique or microscopy of epiluminescence. The main reason is that, due to capture procedure, this technique reduces the reflections of the most superficial layer of the tissue and facilitates the description process of lesions. We have used a database that consists of 98 dermoscopic images, previously diagnosed, 47 of them are benign lesions and 51 are melanomas. To train and to test the system we have used a 10-fold cross-validation method due, essentially, to the reduced number of samples available.

We use classification rate (CR), specificity (SP) and sensitivity (SE) as measures to evaluate the performance of the different methods. The first one represents the portion of samples over the total classified correctly. The specificity is a measure of the per-

Table 1
Algorithm output of the *K* nearest neighbours according to the area size.

Area (K)	CR (%)	SP (%)	SE (%)
5	35.71	31.91	39.22
7	73.47	70.21	76.47
9	70.41	68.09	72.55
11	66.33	63.83	68.63
13	34.69	34.04	35.29

centage which shows healthy cases detected correctly over a total of benign lesions. The sensitivity indicates the portion of melanoma samples detected as right over total of malign lesion samples.

In Table 1 we present the classifying results for kNN algorithm in relation to the area size (k) chosen for the diagnostic. We have used odd sizes to avoid even situation between the two types of the dominium. We can observe that the best classifying results are obtained with an area of size 7, with a classification rate of 73.47% and specificity and sensitivity of 70.21% and 76.47%, respectively.

For the implemented Bayesian classifier we obtained a classification rate of 80.61% and a specificity and sensitivity of 85.11% and 76.47%, respectively.

In Table 2 we can observe the classifying results for a multilayer perceptron taking into account the different number of neurons in the hidden layer. We can observe that the perceptron presents better results when it incorporates more than 6 hidden neurons, being 7 the optimum number: it presents a classification rate of 86.73% and a specificity and sensitivity of 95.74% and 78.43%, respectively.

If we put together these three diagnosis techniques in a collaborative system applying the reliable measures described above and using a vote system to get a consensus in the final diagnosis, we obtain a rate of correct answer of 87.76%, a specificity of 97.87% and sensibility of 78.43%.

We have compared the classifying rates of the individual classifiers and obtained results for the collaborative system. In the Fig. 5 it is possible to observe that the rate of the correct answers of the collaborative system is higher than the other three separated classifiers (acting individually). The measures of specificity and sensitivity are also bigger although they are very similar to the ones offered by the perceptron and the Bayesian classifier.

If we pay attention to the sensibility results of the first technique, they are the lower ones (76.47%), and both the Bayesian classifier technique and the perceptron technique are between 76% and 78%. Nevertheless, the advantage of the Bayesian classifier

Table 2
Output of the multilayer perceptron in relation to the number of neurons in the hidden layer.

Hidden neurons	CR (%)	SP (%)	SE (%)
3	56.12	61.70	50.98
4	60.20	63.83	56.86
5	67.35	72.34	62.75
6	70.41	72.34	68.63
7	86.73	95.74	78.43
8	80.61	87.23	74.51

is that we do not have to adjust any kind of parameter. Meanwhile the multilayer perceptron requires to determinate the values of the different variables interfering in the classification process: the number of hidden layers and the total number of neurons in each of them, the rate of learning, the number of iterations of the backpropagation algorithm, etc. Furthermore, the computational cost of the learning required by the multilayer perceptron is much higher than the Bayesian classifier. In terms of specificity, differences are more marked: from a specificity of 70.21% in the kNN classifier to a 97.87% in the collaborative method. In this case, the high specificity in the perceptron (95.74%) in front of the specificity of easier techniques justifies the selection of the artificial neural network.

One of our objectives was to get a classifier with the sensibility and the specificity balanced. If we get a classifier with a high sensibility but a low specificity, it is not going to be useful as a screening method to avoid biopsies (an invasive technique). And, of course, we want a classifier with a high sensibility to avoid false negatives. Finally, we observe that the collaborative method offers the best results, reaching a specificity of 97.87% and a sensibility of 78.43%.

7. Conclusions and future work

We have presented in this paper a clinical decision support system for melanoma diagnosis using several classification methods working individually and in a collaborative way. We base its logic in a first stage of preprocessing and segmentation by means of Otsu thresholding method. Afterwards, from a set of 24 characteristics that define the injury of the lesion, we obtain an optimum subgroup of six attributes. We have implemented three methods in order to do a classification of the images of skin lesions: the algorithm of the *K* nearest neighbours, a statistics classifier (Bayesian classifier) and a multilayer perceptron. The system, from the subgroup of six descriptors, makes the diagnosis of the input image in two possible classes: benign lesion or melanoma.

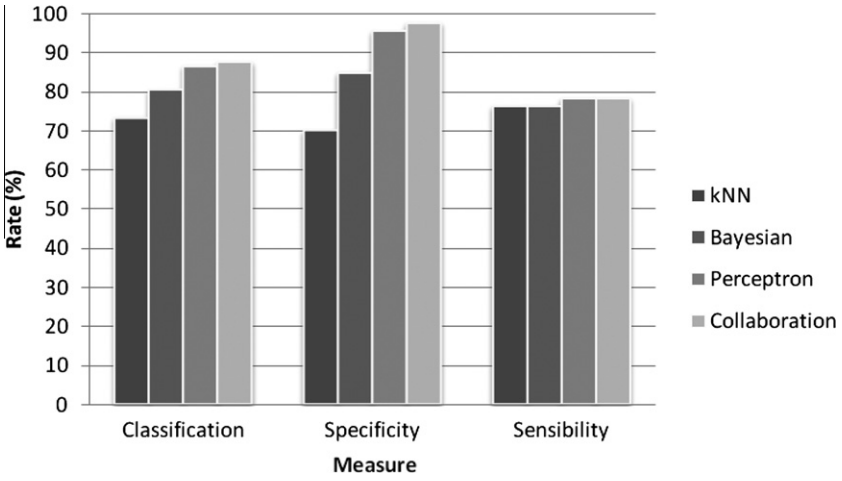

Fig. 5. Comparison of the different classifiers used in the system.

In order to improve the classification rates, we apply the algorithms individually and in a collaborative way thanks to a voting system: each algorithm gives a possible diagnosis decision with a reliability percentage and the system reaches a consensus. The classification rate (87.76%) obtained in the collaborative method is higher than in each method individually.

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