MICROCALCIFICATION EVALUATION IN COMPUTER ASSISTED DIAGNOSIS FOR DIGITAL MAMMOGRAPHY

Joan Martí[1], Joan Batlle[1], Xevi Cufí[1], Josep Español[2]

Abstract

In order to develop applications for visual interpretation of medical images, the early detection and evaluation of microcalcifications in digital mammograms is very important since their presence is often associated with a high incidence of breast cancers. Accurate classification into benign and malignant groups would help improve diagnostic sensitivity as well as reduce the number of unnecessary biopsies. The challenge here is the selection of the useful features to distinguish benign from malignant micro calcifications.

Our purpose in this work is to analyse a microcalcification evaluation method based on a set of shape-based features extracted from the digitised mammography. The segmentation of the microcalcifications is performed using a fixed-tolerance region growing method to extract boundaries of calcifications with manually selected seed pixels. Taking into account that shapes and sizes of clustered microcalcifications have been associated with a high risk of carcinoma based on different subjective measures, such as whether or not the calcifications are irregular, linear, vermiform, branched, rounded or ring like, our efforts were addressed to obtain a feature set related to the shape.

The identification of the parameters concerning the malignant character of the microcalcifications was performed on a set of 146 mammograms with their real diagnosis known in advance from biopsies. This allowed identifying the following shape-based parameters as the relevant ones: Number of clusters, Number of holes, Area, Feret elongation, Roughness, and Elongation.

Further experiments on a set of 70 new mammograms showed that the performance of the classification scheme is close to the mean performance of three expert radiologists, which allows to consider the proposed method for assisting the diagnosis and encourages to continue the investigation in the sense of adding new features not only related to the shape.

Keywords: Microcalcifications, shape-based features, image segmentation

1 Introduction

In the western countries, breast cancer is the leading cause of death in women between 40 and 55 years of age. In the Regional Health Area of Girona, the estimated incidence during 1996 was 83

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new cases for 100.000 women/year of infiltrating breast carcinoma. At present the mammogram is the only proven method for detecting minimal breast cancer[1]. One important indicator of breast cancer is the presence of clustered microcalcifications. Clustered microcalcifications can be seen on mammograms in 30% - 50% of cases of breast cancer. However, most mammografic calcifications are benign. Accurate classification of microcalcifications into benign and malignant groups would help improve diagnostic sensitivivy as well as reduce the number of unnecessary biopsies.
Microcalcifications usually appear as small, bright, arbitrarily shaped regions on the large variety of the breast texture background. Thus, their analysis and characterization are performed throughout the extraction of features[2] and visibility descriptors[3] by means of several image processing techniques, such as gray-level image analysis[4], signal processing algorithms[5] or morphological methods[6]. Statistical techniques are later used in order to evaluate the obtained features and their ability to properly characterize the malignant or benignant character of the microcalcifications.

2 Materials and Methods

The proposed microcalcification evaluation method consists of several stages, as outlined in figure 1.

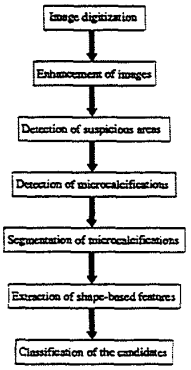

Figure 1: Overview of the microcalcification evaluation method

A set of 146 mammograms was used at the retrospective stage with the goal to analyse the incidence of features in the malignant character of the microcalcifications and therefore, to choose the best features in order to build a statistical predictive model for the malignant diagnosis. The real diagnosis was known in advance from biopsies. The medical diagnosis for the retrospective mammograms, issued by expert radiologists and oncologists, are known.
The predictive model was tested at a prospective stage, composed by 70 mammograms not diagnosed in advance. In order to evaluate the performance of the selected features for characterizing the microcalcifications and the power of the statistical model, the diagnosis provided by the model was compared to the real diagnosis given by the biopsies. Finally, this evaluation was compared to the diagnosis issued by 3 expert radiologists.

2.1 Image Digitization

Conventional mammograms, in which the positions of clustered microcalcifications were determined by well experienced radiologists, were digitized using a CCD camera at a pixel size ranging from 12 to 37 micrometers and a twelve-bit gray scope, producing a 1524x1012 matrix image. An unshap-mask filter was applied to enhance the high-frequency component on the digitized images, only to make it easier for the observers to recognize the microcalcifications at the stage of annotated image display.

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The whole set of digitized mammograms composes an unpublished database formed by patients of the Regional Health Area of Girona, now available upon request, which in the future may contribute to increase the digital mammogram databases.

2.2 Image Segmentation

The microcalcifications are segmented using a region-growing algorithm based on *Shen* segmentation techniques[7]. The algorithm starts with a selected pixel inside every microcalcification, called the seed pixel, which has been manually selected by the expert radiologists. This becomes the first region pixel; then, pixels $p(i,j)$ of every 4-connected neighbor of pixels belonging to the region, are checked for the tolerance-region condition:

$$(1+\tau)(F_{max}+F_{min})/2 \geq p(i,j) \geq (1-\tau)(F_{max}+F_{min})/2 \quad (1)$$

where F_{max} and F_{min} are the current maximum and minimum pixel values of the growing region, and τ is the growth tolerance ($0 \leq \tau \leq 1$). This recursive procedure is continued until no connected pixel meets the condition expressed in (1). Stating that the major difficulty of this method is the determination of the tolerance value for each calcification, a multi-resolution procedure is used, trying to find the most appropriate tolerance value τ for each microcalcification.
A tolerance value τ is selected for each region. The final choosen value is selected among the candidates ranging from 0.01 to 0.4 with a step increment (SS) determined by the seed pixel (SP) value as $SS = 1/SP$. For every region obtained at each tolerance level a feature set is calculated, including shape compactness, centre of gravity (x,y) coordinates, and size (number of pixels). The normalized distance of this feature set among the successive tolerance levels is computed, and the feature set with the minimum distance is selected as the final set in order to choose the value of τ.

3 Shape-based Feature Set

After segmenting the microcalcifications in every digitized mammogram, a set of binary regions was obtained in each image. The characterization of these regions is not a trivial task, although several methods have been proposed in the literature[8]. Taking into account that shapes and sizes of clustered microcalcifications have been associated with a high risk of carcinoma based on different subjective measures, such as whether or not the calcifications are irregular, linear, vermiform, branched, rounded or ring like, our efforts were addressed to obtain a feature set related to the shape.

3.1 Initial Feature Set

Early analysis of the data revealed that, among other shape-based features, the following features play a significant role: `Area` (number of pixels in the microcalcification), `Compactness` (derived from the perimeter —P— and the area —A—, it is equal to $\frac{P^2}{4\pi A}$, `Number of holes per area` (the number of holes in the microcalcification), `Feret Elongation` (a measure of the shape of the microcalcification), `Roughness` (a measure of the roughness, it is equal to $\frac{Perimeter}{ConvexPerimeter}$, and `Principal Axis` (the angle at which a microcalcification has the least moment of inertia —the axis of symmetry—). Additionally, the number of clusters for each mammogram was added to the subset, stating that a cluster is defined when 4 or more microcalcifications are found in an almost circular area with a diameter = 0.5 cm.

3.2 Statistical Parameters

From the previous subset of features, some statistical parameters were calculated in order to resume

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the information contained in the microcalcifications of a mammogram: mean (m), median (med), standard deviation (s), coefficient of variation (cv), minimum (min), and maximum (max).
From an initial exploratory analysis of the statistical parameters of the feature variables over the retrospective mammograms, a high bias was observed in the histogram of the means of most of these variables. This fact suggested the convenience to apply the logarithm transformation to the biased variables. In addition, the minimum and the maximum of the feature variables seemed to be useless due to their high variability. It was considered more informative to take into account the number of "outliers" ($nout$) of these variables in each mammogram (a value of a feature variable was considered to be "outlier" or "anomalous" if it was more than 3 standard deviations away from the global mean).

3.3 Predictive statistical model

Using the *logit* function as a link function of the logistic regression model, the *odds ratio* of the variables `n.micr` and `n.clus`, and of the statistical parameters of feature variables has been calculated from the information given by the 146 mammograms of the retrospective stage. From the calculated odds ratio, it has benn be observed that the probability of malignacy of a mammogram with suspicious microcalcifications increases when the number of microcalcifications, the number of clusters and the number of anomalous microcalcifications (outliers) related to the feature variables `n.hol/ar`, `l.fer.elon`, `l.rough`, `l.elon` and `l.comp` also increases. This probability also increases if the ratio `n.hol/ar` increases, but decreases if the area of the microcalcifications increases. It is also important to state that the odds ratios of the standard deviation s of the feature variables related to the shape of the microcalcifications (`n.hol/ar`, `l.fer.elon`, `l.rough`, `l.elon`, `l.comp`) are all greater than 1. This fact shows that the more heteregoneus are the microcalcifications of a mammogram the higher is the probability of malignacy.
The models *logit* and *normit/probit* were tested to build predictive logistic regression models from the 146 mammograms of the retrospective stage. From the comparison of the associated ROC (Receiver Operating Characteristic) curves, the *normit* model was choosen. This model provides the probability p_i according to the equation

$$\Phi^{-1}(p_i) = \beta_o + \beta_1 X_{1i} + \cdots + \beta_k X_{ki} \qquad (i = 1, \ldots, n) \tag{2}$$

where Φ represents the distribution function of a normal standard rule.
The selection of the best model was made using a stepwise procedure over the entire set of retrospective mammograms. For each mammogram, a 99% confidence interval of the malignacy probability was estimated. According to that, each mammogram was classified as *absolutely benignant* (`bb`), *absolutely malignant* (`mm`) or *benignant-malignant* (`bm`) depending on whether its confidence interval was completely included in the range $0 - 0.50$, or in the range $0.50 - 1$, or contained the 0.50 value, respectively.

4 Experimental Results

The model has been tested on the prospective mammograms in order to check the performance of the selected features choosen by the statistical predictive model to estimate the malignacy of the microcalcifications of a mammogram. Like in the retrospective stage, the mammograms were classified as *absolutely benignant, absolutely malignant* or *benignant-malignant*. Table 1 illustrates the results obtained over the 70 mammograms that compose the prospective data, comparing the result of this classification with the diagnosis given by the biopsies.

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		Predicted by the model			
		bb	bm	mm	All
Diagnosis from biopsy	Benignant	19	27	3	49
		38.78	55.10	6.12	100.00
		90.48	72.97	25.00	70.00
	Malignant	2	10	9	21
		9.52	47.62	42.86	100.00
		9.52	27.03	75.00	30.00
	All	21	37	12	70
		30.00	52.86	17.14	100.00
		100.00	100.00	100.00	100.00

Table 1: Comparative results between the diagnosis predicted by the statistical model and the diagnosis from biopsies (cell contents: counts, % of row, % of column)

The ROC curve associated to these 70 prospective mammograms is shown in figure 2. As it was foreseable, the results are not as satisfactory as with the retrospective mammograms, because the proposed model classifies incorrectly 5 mammograms (7.05%), classifies correctly 28 mammograms (40%) and does not decide on 37 mamograms (52.86%).

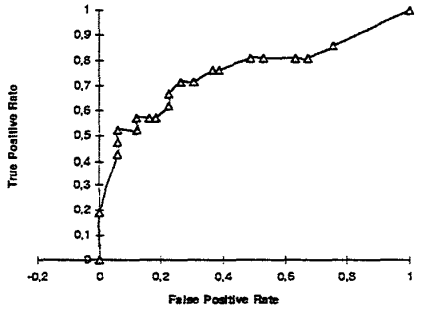

Figure 2: ROC curve for the prospective data with the proposed model

As a final performance evaluation, the classification scheme provided by the model was compared with the diagnosis issued by three expert radiologists, which indicated the malignant character of the mammogram based on the microcalcifications appearance. Over the 49 benignant mammograms diagnosed by the radiologists, 2 cases (4.08%) were diagnosed incorrectly, 25 cases (51.02%) correctly, and for 22 cases (44.90%) no clear diagnosis could be established. The proposed model misclassifies 3 cases (6.12%), classifies correctly 19 cases (38.78%) and does not decide in 27 cases (55.10%). The same conservative behavior is observed over the 21 malignant mammograms that complete the prospective set: while the diagnosis provided by the radiologists is incorrect in 3 cases (14.29%), correct in 12 cases (61.90%), and does not decide in 5 cases (20.81%), the proposed model classifies incorrectly 2 cases (9.52%), correctly 9 cases (42.86%) and does not decide in 10 cases (47.62%).

5 Discussion and Conclusion

The purpose of this study was to select a set of shape-based features for characterizing microcalcifications in order to assist radiologists in classifying malignant and benignant clustered microcalcifications

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in mammograms. The use of statistical parameters have allowed to choose the significant features used in the model: area, number of holes per area, Feret elongation, roughness, elongation, compactness, and principal axis.
The results obtained have shown that the use of shape-based features potentially improve the radiologists' diagnostic performance by increasing the sensitivity value, when the classification scheme results confirm, elevate, or initiate a radiologist's suspicion regarding a malignant lesion which might otherwise be misinterpreted as benign. The performance of the classification scheme is close to the mean performance of three expert radiologists, which allows to consider the proposed method for assisting the diagnosis and encourages to continue the investigation in this field.

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