Original paper

Discrimination of malignant and benign microcalcification clusters on mammograms

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Abstract: In this paper a new classification method of clustered microcalcifications by using the weighted wavelet transform technique in digitized mammograms is introduced. The new method uses three types of indicators of malignancy, i.e., (1) the standard deviation of the densities of individual microcalcifications within a cluster, (2) the coefficient of variation of their sizes within a cluster, and (3) the circularity of a cluster. The method was applied to the evaluation of malignancy of 35 microcalcification clusters taken as somewhat difficult cases from Breastpia Namba Hospital's patient files by an experienced mammographer. The results of the discriminant analysis using these indicators showed 95.24% of sensitivity and 78.57% of specificity.

Keyword:Microcalcification, Mammogram, Classification

1 Introduction

Mammography is the most sensitive method for the detection of early breast cancer. However its efficacy is limited by the poor positive predictive value (15-30%) obtained by human observer [Adler 92, Kopans 91]. One of the potential approaches to improve the specificity of mammography may be the use of computer-aided diagnosis (CAD) scheme. They can automatically extract image features from the regions of interest (ROI) and estimate the likelihood of malignancy for a given lesion, thereby providing the radiologist with additional information for making diagnostic decisions easier.

Since microcalcifications are important indicator of early breast cancer, a number of investigators have developed feature extraction and classification methods to characterize microcalcifications. Shen *et al.* used 3 shape features, compactness, moments, and Fourier descriptors to classify individual microcalcifications [Shen 94]. Jiang *et al.* trained a neural network classifier to analyze 8 features extracted from microcalcification clusters [Jiang 96, Jiang 99]. Chan *et al.* developed morphological and texture features and evaluated various feature classifiers for differentiation of malignant and benign microcalcifications [Chan 97, Chan 98]. Although the results of these studies are expected to depend strongly on data set, they indicate that the CAD techniques have a potential to improve the diagnostic accuracy.

Various types of calcification can be seen in mammograms. Among these, clustered microcalcifications are the most difficult to analyze accurately and are the main cause of ensuing biopsies. This paper therefore concentrates on the analysis of clustered microcalcifications. To classify lesions into malignant and benign, we use here three features. Two of them are the heterogeneity of the shapes and size within a cluster, which are known to be major criteria for differentiation of malignant and benign microcalcification clusters [Kopans 98]. An-

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(a) Original image (b) Segmented image (c) Cluster margin

Figure 1: The processes for estimating the margin of a cluster.

other one is the indicator about the spatial distortion of the microcalcifications as a group, since the calcification associated with breast cancer is sometimes guided along with the duct, resulting somewhat distorted distribution. The following sections will present the details of these features, and will estimate the accuracy of our CAD scheme.

2 Materials and Methods

2.1 Experimental data set

Thirty magnification mammograms with clustered microcalcifications were selected by an experienced mammographer from the patient files in the Breastpia Namba Hospital. This selection was performed with a criterion that each cluster was very difficult to classify its malignancy without biopsy. There were 21 malignant and 14 benign clusters which were diagnosed through biopsy. The locations of the microcalcification clusters on each mammogram were also identified by the radiologist, and only the true microcalcification clusters were the target of present study. All the magnification mammograms were digitized at a resolution of 50 μm/pixel, 12bits (4096 gray levels) using an ES-8000 digitizer supplied by EPSON.

2.2 Segmentation of individual microcalcifications

In our previous paper [Uchiyama 99] we have developed a program to detect microcalcifications using weighted wavelet transform. As was shown in [Uchiyama 99], the program can extract local convexes of given sizes effectively and can enhance microcalcifications selectively while maintaining the details of their shapes. However, if we determine a threshold to get 100% of detection sensitivity, then the detected signals also include false positives. These false positives were erased manually, since the present purpose of this study is to examine the discrimination power of the new indicators of malignancy from benign microcalcifications. We use the term "segmented image" as each of the true positive microcalcification in this paper.

2.3 Defining a cluster and its margin

To each microcalcification a center of gravity was determined to which a circle of radius of 50 pixels was drawn. If any of these circles have instances of overlapping, then we consider them forming a same cluster(Fig.1). And the margin of the cluster is defined as the outermost edges covered by these circles within a cluster.

2.4 Feature extraction

All calcifications associated with breast cancer form in the intra-ductal portion of the cancer. Although

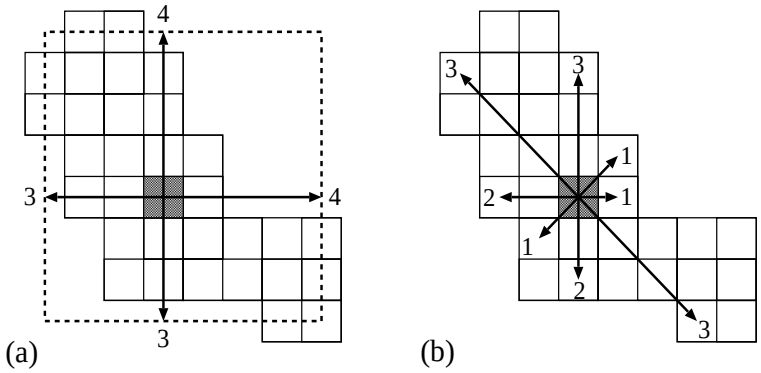

Figure 2: Illustrations of the 12 shape indexes. (a)A smallest rectangular box that enclosed the cluster was first drawn (dashed lines), and the distances between the center-of-cluster pixel (shaded) and the boundary of the rectangular box forms the first four shape indexes (depicted by arrows in Fig.2a). (b)Eight shape indexes are the maximum lengths of straight lines drawn from the center-of-cluster pixel (shaded) to the outermost pixels in the cluster in eight directions (arrows).

the multiplying cells can expend the duct, the necrosis usually occurs irregularly in the center of the duct. The cells in the center become hypoxic as their distance from their blood supply increases and eventually the center of the tumor becomes necrotic. Because this is an irregular process at the center of the intra-ductal cancer, the calcifications formed are very small, irregular, and haphazard. Their distribution is guided by the course of the duct, giving a very distinctive linear, branching pattern. This pattern of calcium distribution is due to comedo-necrosis. Suspicion should be aroused when a group of calcifications is very heterogeneous [Kopans 98]. In this study, three features were selected by us on the basis of the characteristics of calcifications described above. These features are: (1)the standard deviation of the densities of individual microcalcifications within a cluster (SD), (2)the coefficient of variation of their sizes within a cluster (CS), and (3)the circularity of a cluster margin (CM). The first two features were used to characterize the shape or size irregularity of individual microcalcifications. While the last one was used to express the spatial distribution of the microcalcifications as a group. The detailed descriptions of these features are as follows.

2.4.1 Standard deviation of the density (SD)

Each cluster contains several microcalcifications. The density of each microcalcification, I_k, was given as the mean of top 5 pixels in gray level. The standard deviation of them in a cluster is defined in the usual manner as

$$SD = \sqrt{\frac{1}{N}\sum_{k=1}^{N}(I_k - \bar{I})^2}.$$

Here N is the number of microcalcification in a cluster, and $\bar{I}$ is the mean value of I_k.

2.4.2 Coefficient of size-variation (CS)

The size of a microcalcification, A_k, was measured by counting the number of all pixels within its segmented image. Then, the coefficient of variation of the sizes is defined as.

$$CS = \frac{1}{\bar{A}}\sqrt{\frac{1}{N}\sum_{k=1}^{N}(A_k - \bar{A})^2}.$$

Here, N is the number of microcalcification within a cluster, and $\bar{A}$ is the mean value of A_k.

2.4.3 Circularity of a cluster Margin (CM)

The circularity of a cluster was evaluated by using 12 shape indexes [Jiang 96]. Four shape indexes represent distances between the center-of-cluster pixel and the boundaries of the minimum rectangular in which the cluster is included. Another eights shape indexes were the lengths of straight lines from the

center-of-cluster pixel to the pixels located in the outermost positions in eight directions within the cluster (see Fig.2).

The coefficient of variation of these 12 shape indexes was used to characterize the circularity of the cluster, that is

$$CM = \frac{1}{\bar{SI}}\sqrt{\frac{1}{12}\sum_{k=1}^{12}(SI_k - \bar{SI})^2}.$$

where SI_k is a shape index, and $\bar{SI}$ is the mean of 12 shape indexes. For a compact (round) cluster, all 12 shape indexes have the same value, and their coefficient of variation becomes zero. For an irregular (linear or branching) cluster, some of the 12 shape indexes have large values, keeping others small, which results in large coefficients of variation.

3 Results

Figure 3 shows the distributions of the three features for 35 clusters of microcalcifications in 30 mammograms. Figure 3(a) is a scatter plot of each cluster. The x-axis is the value of CS, while the y-axis is those of SD. Figure 3(b) is a distribution of the circularities of the cluster margin (CM). To know how each feature contributes to the discrimination we performed the multi-variate discriminant analysis by using SPSS statistical package [SPSS]. Table 1 shows the group means and the standard deviations, while table 2 is the tests for univariate equality of group means.

Table 2 indicates that CS greatly contributes to the difference of two groups. And CM comes next while the value of SD would make little to this discrimination. To know the interdependence among these variables, a pooled with-in groups correlation matrix was evaluated (Table3).

From Table 3 it is known that the values of CS and CM correlate somewhat strongly, which means CM would not contribute so large to the difference of two groups as was expected from Table 2 when used together with CS. Table 3 also indicates that SD is an independent variable. Table 4 is the unstandardized and standardized discriminant func-

Group	Mean	Standard Deviation	Number
Benign CM	10.2223	5.0716	14
Benign SD	223.8898	112.5862	14
Benign CS	59.8648	14.3875	14
Malignant CM	17.8313	7.0671	21
Malignant SD	288.6721	118.9299	21
Malignant CS	89.0158	17.5767	21

Table 1: Simple Statistics

Variable	Wilks' Lambda	F	significance
CM	0.733	12.038	0.001
SD	0.927	2.599	0.116
CS	0.554	26.557	0.000

Table 2: Wilks' lambda and univariate F-ratio with 1 and 33 degree of freedom.

	CM	SD	CS
CM	1.000	0.033	0.334
SD	0.033	1.000	-0.031
CS	0.334	-0.031	1.000

Table 3: Pooled within-groups correlation matrix

	unstandardized	standardized
CM	0.062	0.329
SD	0.003	0.295
CS	0.049	0.799
constant	-5.198	

Table 4: Discriminant function coefficients

Benign (Specificity)	11/14 (78.57%)
Malignant (Sensitivity)	20/21 (95.24%)

Table 5: Percentage of cases classified correctly

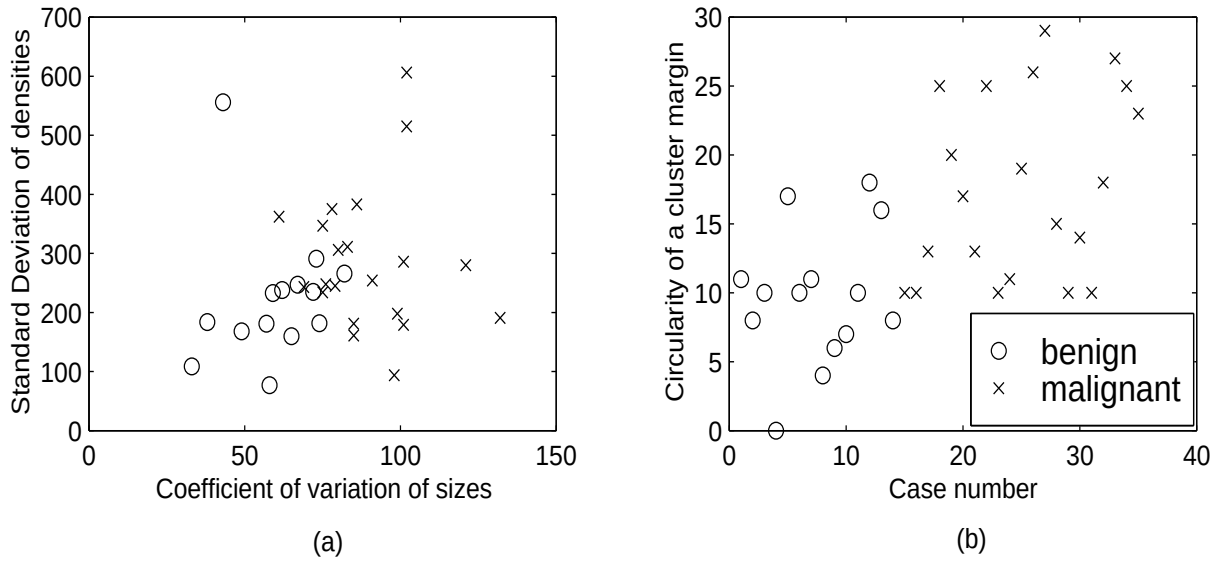

Figure 3: Diagrams of the distributions of malignant and benign clustered microcalcifications for three features. (a)The standard deviation of the densities and the coefficient of variation of sizes. (b)Circularity of cluster margin.

tion coefficients, and Table 5 is the percentage of cases classified correctly.

4 Discussion

Although all cases used were very difficult to diagnose their malignancy without biopsy, we made receiver operating characteristic (ROC) analysis to check objectively the difficulty of cases. We asked another experienced specialist for mammography diagnosis to diagnose malignancy through mammograms. He knew nothing about the patients except the images offered by us. To each case we made two images of mammogram, i.e., full scale image of a mammogram in which ROI is depicted, and the enlarged image of ROI. In the creation of the enlarged image, care was taken in the calibration of the window level so that each microcalcification is most clearly shown. These two images of each case are put into the Microsoft Power-Point Viewer, which might make diagnosing more difficult, since there is no tool to change the windows level. Figure 4 is the result of this ROC analysis. The eigen-value, which is the ratio of between-groups sums of square and within-groups sums of square, was 0.995. This extremely high eigen-value also supports the goodness of the obtained discriminant function in the cases used. Many investigations have been done in the past to obtain good indicators or features for the discrimination of malignant and benign microcalcifications, and the features introduced in this paper should be fully examined in the past. We wondered why we could discriminate so wonderfully in these difficult cases. Two reasons we can think of. One is the use of the weighted wavelet transform, by which we can extract only the micro-convexes in a mammogram. The features evaluated by using this transform might reflect correctly the characteristics of each microcalcification. The second is about the number of cases. Thirty-five may not be sufficient to believe that the present results is statistically significant. Although the number of cases is small to make statistically significant conclusions, however, it will be possible to say that (1) all cases used are very difficult to diagnose, and (2) there is high possibility to make good CAD scheme by using the present method.

5 Concluding Remarks

In this paper, we proposed a candidate of good CAD scheme for supporting diagnosis of mammograms by using the weighted wavelet transform technique for extraction of microcalcifications and three features obtained from them. These features are selected by experienced mammographer on the basis of the

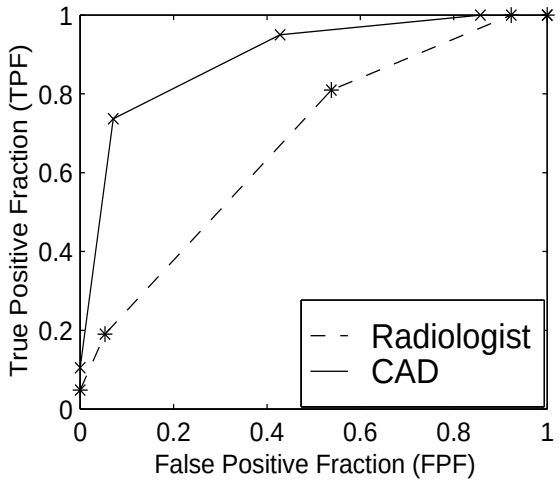

Figure 4: The results of ROC analysis

characteristics of microcalcification associated with cancer. We applied them to 35 cases of patient files. All of them were difficult to diagnose their malignancy without biopsy. SPSS statistical package was used for discrimination. The experimental results shows very high values of sensitivity (95.2%) and of specificity (78.6%) to the cases examined.

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微細石灰化クラスタの良悪性鑑別システム

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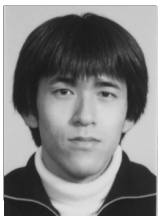
要旨：この論文では、マンモグラムにおける微細石灰化クラスタに対する良悪性鑑別の新しい手法を提案する。本手法は、３個の特徴量を用いて鑑別を行う。これらの特徴量は、(１) クラスタ内に存在する石灰化の濃度の標準偏差、(２) クラスタ内に存在する石灰化の面積の変動係数、(３) クラスタ領域の円形度である。これらの３個の特徴量に対して判別分析を用い、ブレストピアなんば病院のマンモグラムの中からマンモグラフィ読影医により選択された鑑別の非常に困難な微細石灰化クラスタ３５例を対象に良悪性鑑別を試みた。その結果、真陽性 (悪性石灰化クラスタを悪性と鑑別) 率 95.24%、真陰性 (良性石灰化クラスタを良性と鑑別) 率 78.57% という結果が得られ、本手法の有効性を確認した。



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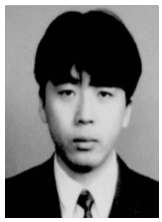

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