CHARACTERIZATION OF CLUSTERED MICROCALCIFICATIONS IN DIGITIZED MAMMOGRAMS USISNG NEURAL NETWORKS AND SUPPORT VECTOR MACHINES

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Characterization of Clustered Microcalcifications in Digitized Mammograms using Neural Networks and Support Vector Machines

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Abstract

We have developed an automated method for the characterization of microcalcification clusters in digitized mammograms as malignant or benign. The proposed method has been implemented in three stages: (a) the cluster detection stage to identify clusters of microcalcifications, (b) the feature extraction stage to compute the important features of each cluster and (c) the classification stage, which provides with the final characterization. In the classification stage an expert rule-based system, a neural network and a support vector machine (SVM) were implemented and evaluated using ROC analysis. We have conducted experiments using the Nijmegen database. The original feature set was enhanced by the addition of four rule-based features. The performance of SVM was A_z=0.77 and A_z=0.79 for the original and enhanced feature set, respectively, while the corresponding performance of the neural network was A_z=0.70 and A_z=0.76.

Keywords- Support vector machines, Neural network, Classification, Microcalcification cluster, mammography

1 Introduction

Several methodologies have been developed in order to improve radiologists' efficiency in the diagnostic interpretation of mammograms. The successful development of CAD (Computer Aided Diagnosis) systems will be of great value, when these systems are used as second opinion to the radiologist. CAD systems integrate image analysis and artificial intelligent techniques aiming at providing with accurate, objective and reproducible mammogram interpretation procedures.

The problem of mammogram interpretation using CAD systems can be decomposed into two sub-problems. The first deals with the detection and localisation of regions of interest (ROIs), which include suspicious lesions. The second and the more difficult sub-problem is the characterization of the identified lesions as malignant or benign (LANYI, 1988). Such a successful characterisation can contribute to the reduction of unnecessary biopsies.

The most common approach for the development of CAD systems includes feature extraction algorithms materialized either using computer systems or through manual extraction by radiologists (BAKER *et al.*, 1995; WU *et al.*, 1993) that compute important features subsequently fed into a classifier. Automatic feature extraction procedures utilize image analysis techniques for the computation of feature vectors characteristic of structures detected at the segmentation stage. Several types of feature extraction methods can be found in the literature such as morphological (TAYLOR *et al.*, 1999; NAKAYAMA *et al.*, 1999; DENGLER *et al.*, 1993; ZHAO, 1993), texture (CHAN *et al.*, 1998; ROGOVA *et al.*, 1999; MEERSMAN *et al.*, 1998), fractal (LEFEBVRE

et al., 1995, LI *et al.*, 1997), histogram statistics (GAVRIELIDIS *et al.*, 2000) and wavelets (YU *et al.*, 2000; STRICKLAND *et al.*, 1996; WANG *et al.*, 1998; YOSHIDA *et al.*, 1994). Morphological features are the most commonly used due to their similarity with the characteristics taken into account by the radiologists.

Several methodologies have been presented for the lesion characterization problem, such as decision trees (TAYLOR *et al.*, 1999, BOTTEMA *et al.*, 2000), linear discriminant classifier (CHAN *et al.*, 1998; NAKAYAMA *et al.*, 1999), k-nearest neighbours (VELDKAMP *et al.*, 2000; SOLTANIAN *et al.*, 2001) and neural networks (BAKER *et al.*, 1995; WU *et al.*, 1993; JIANG *et al.*, 1996a; JIANG *et al.*, 1996b; Schmidt *et al.*, 1999; SHEN *et al.*, 1994; LEE *et al.*, 2000; HARA *et al.*, 2001; VERMA, 1999). In general it is very difficult to compare the efficiency of the above methods since they have been tested in different mammographic datasets using different performance measures.

In this work an automated system for the characterization of microcalcification clusters as malignant or benign is presented. The method consists of three stages: the cluster detection stage described in an previous work (PAPADOPOULOS *et. al.*, 2002), the feature computation stage and the final classification stage. Two different classification schemes have been implemented and tested based on neural networks and SVMs. It must be noted that SVMs are used for the first for the cluster characterization problem. Originally, among a set of 54 features we have selected 33 of them. In addition, we have defined a new type of features, called rule-based features, which are obtained using 2D graphical representation with respect to all pairs of features. This resulted in an enhanced feature set consisted of 37 features.

The performance of the classifiers has been evaluated using the receiver operating characteristic (ROC) methodology (METZ, 1986) and the classification rate. The obtained results are very encouraging and thus our method can be considered very promising.

2 Materials and Methods

2.1 Image Dataset

We use the Nijemegen mammographic image database (KARSSEMEIJER, 1993). It consists of 40 images of both craniocaudal (CC) and oblique (MLO) views from 21 patients. The digitisation sampling aperture is 0.05 mm and the sampling distance 0.1 mm and the size of each image is 2048 × 2048 pixels. 12 bits are used for each pixel representation and we have rescaled the images to 8 bit depth (256 grey levels) using a noise equalization table set which it is provided with the database. The microcalcification clusters have been annotated in each image by expert radiologists using a circle enclosing the abnormality. The total number of annotated clusters is 105, which correspond to 76 malignant and 29 benign microcalcification clusters.

The proposed method for the characterization of the microcalcifications as malignant or benign has been implemented in three stages. Initially, a cluster detection procedure is used to identify clusters of microcalcifications. Next, important features of those clusters are computed. In the final stage the features are used as input to a classification system to provide with the final diagnosis.

2.2 Cluster Detection Procedure

The objective of this stage is the identification of clusters of microcalcifications. The procedure we followed has been described in an earlier work (PAPADOPOULOS *et al.*, 2002) and is based on a hybrid intelligent system combining rule-based and neural network methods. Fig. 1 shows the sequential stages of the detection procedure. Initially, a pre-processing procedure is applied in order to remove the useless radiological marks as well as the background of the image. Then, background correction along with contrast enhancement are applied to indicate potential microcalcification objects. Morphological descriptors are used to extract the regions of interest (ROIs). Then, for all objects and clusters contained in every ROI we compute several discriminating morphological and textural features, which are used as input to the classification system. This system is a hybrid intelligent system based on a combination of a rule-based and a neural network component providing with characterization of the ROI as cluster of microcalcifications or not. For the Nijmegen database the detection module provides 115 regions of interest corresponding to 80 malignant and 35 benign clusters.

2.3 Features Computation and Selection

For each detected cluster 54 features have been identified, which are shown in Table 1. Those features refer either to an individual microcalcification (microcalcification feature) or as averages of the five largest microcalcifications included in a cluster (cluster feature).

In order to reduce the number of features a feature selection procedure based on ROC analysis has been followed to identify the most discriminative features. The ROC curve (METZ, 1986) has been plotted for each feature and the area A_z under the curve

is computed. Using a quite low threshold value $A_z = 0.52$ we selected 33 features having A_z value higher than the threshold. The majority of features are the same to the features used for the detection procedure described above. The use of extra features underlines the increased difficulty of the classification of the clusters to benign or malignant compared to the removal of the false positive detected samples.

2.4 Classification methods

The aim of the classification process is the characterization of each cluster as malignant or benign using the selected features. In this work we have employed rule based expert systems, neural networks and support vector machines.

2.4.1 Rule based expert system

The common approach in this class of systems includes the use of rules applying thresholds is selected features. However, in our case it is not possible to define discriminative rules of this type. Thus, we followed the following approach: Initially, a 2-D graphical representation of the dataset in two feature space has been performed for each pair of features (e.g. see Fig. 2). It was understood that four of those plots have the highest discriminative value. That means that in the two feature space a straight line (defining a linear decision rule) can be drawn which defines a region (half space) containing mostly (more than 90 %) points belonging to the same class. The pairs of features corresponding to those plots are: (a) mean microcalcification cluster eccentricity – mean contrast, (b) mean local background – mean distance from cluster centroid, (c) mean contrast - mean compactness and (d) standard deviation of the microcalcification distances from the cluster centroid – equivalent diameter of the cluster.

This set of rules cannot be used as an independent classifier due to its poor performance (see Table 2). However, the distance of a point from the corresponding linear boundary constitutes an additional feature to be used in the classification system. It must be also noted that each of these distance features has a sign which indicates the half space in which the data point lies. The incorporation of the additional four features into the initial set of selected features results in an enhanced feature set (it consists of 37 features).

2.4.2 Neural Classifier

The neural network classifier we have used is a feedforward network with sigmoid hidden nodes (Multilayer Perceptron – MLP). The selected neural network architecture consists of one hidden layer with fifteen sigmoid nodes, and an output layer with one sigmoid node, whose value indicates malignant or benign microcalcification cluster. Principal component analysis (PCA) is implemented in order to reduce the size of the input feature vector. The output of the PCA is an reduced feature vector composed of seven features that contribute more than 3% of the total variation of the original feature set. Those features are normalized to zero mean and unit variance. Gradient decent, resilient backpropagation, conjugate gradient and quasi-Newton methodologies were employed for neural network taining in order to select the one with the best classification ability (BISHOP, 1996). The training procedure is terminated either when that training error is less than 10^{-5} or when 2000 iterations have been performed. The highest performance was obtained using quasi-Newton one-step-secant (OSS) algorithm (BATTITI, 1992). The two fold cross validation method is utilized for the performance assessment. When the

enhanced feature set is used the classification performance, using the same neural network architecture and PCA, is improved.

2.4.3 Support Vector Machines

Another category of classification methods that has received special attention recently is the Support Vector Machines (BURGES, 1998; CRISTIANINI *et al.*, 2000). SVMs have not used previously for clusters of microcalcification characterization but only for their detection (BAZZANI *et al.*, 2000; EL-NAQA *et al.*, 2002). SVMs are based on the definition of an optimal hyperplane, which linearly separates the training data so that minimum expected risk is achieved. In contrast with other classification schemes, an SVM aims to the minimization of the empirical risk R_{emp} and at the same time, the maximization of the distances (geometric margin M) of the data points from the corresponding linear decision boundary (Fig. 3). R_{emp} is defined as $R_{emp}(a) = \frac{1}{2l}\sum_{i=1}^{l}|y_i - f(x_i,a)|$, where $x_i \in R^N$, $i=1,...,l$, is the training vector belonging to one of two classes, l is the number of training points, $y_i \in \{-1,1\}$ indicates the class of x_i, and f is the decision function. The training points in the space R^N are mapped nonlinearly into a higher dimensional space F by the function (*a priori* selected) $\Phi: R^N \rightarrow F$. In this space (feature space) the decision hyperplane is computed. The training algorithm uses only the dot products ($\Phi(x_i) \cdot \Phi(x_j)$) in F. If there exists a "kernel function" K such that $K(x_i,x_j)=\Phi(x_i)\cdot\Phi(x_j)$, then only the knowledge of K is required by the training algorithm. The decision function is defined as

$$f(x) = \sum_{i=1}^{l} y_i a_i K(x_i, x) + b$$

where a_i are the weighting factors and b denotes the bias. After training, the condition $a_i>0$ is valid for only a few examples while for the others it holds that $\alpha_i = 0$. Thus the final discriminant function depends only on a small subset of the training vectors which are called support vectors.

The selection of the kernel K is of major importance for the performance of the classifier. Several types of kernels have been reported in the literature, such as the polynomial type of degree p, $K(x_i, x) = (x_i \cdot x + 1)^p$ and the Gaussian kernel $K(x_i, x) = e^{-|x_i - x|^2 / 2\sigma^2}$ (σ is the kernel width). Each kernel function should fulfill *Mercer's condition* (BURGES, 1998; VAPNIK, 1995).

We use the SVM algorithm provided by the LIBSVM library (CHANG *et al.*, 2002), which has been proven that is stable, computationally inexpensive and highly competitive compared with other SVM codes [PLATT, 1998; KEERTHI *et al.*, 1999; JOACHIMS, 1998; CHANG *et al.*, 2001,).

We have tested the Gaussian kernel for several values of the standard deviation σ. In order to apply the SVM training algorithm the following parameters must be adjusted: the regularization parameter C and the termination criterion ε. To perform parametrization we have applied the training algorithm for the following values of the parameters: $\gamma \in \{10^{-5}, 10^{-4}, \ldots, 0.01, 0.5\}$, $C \in \{1, 10, \ldots, 10^5\}$ and $\varepsilon \in \{10^{-5}, \ldots, 10^{-1}\}$.

3 Experimental Results

The above described methodology is evaluated on the Nijmegen mammographic dataset. The database reference file reports 105 cluster areas. Applying the detection algorithm we have identified 15 more areas because in some cases two separate ROIs had been detected into one database annotated circle. From the total 120 ROIs, 84 are malignant and 36 are benign. To assess the performance of our method we have employed ROC analysis (computation of A_z). Moreover, in order to compare our results with previous reported we have computed the best classification rate (BCR=ratio of the sum of true positives and true negatives over the total number of samples) for a range of threshold values.

For the rule based classifier, if a decision rule is valid then the cluster is classified as malignant, otherwise as unclassified. Using the expert system with the four linear decision rules we achieved the correct characterization of 44 (52%) malignant clusters and the false characterization of 2 (5.8 %) benign. The decision is based on the majority voting, using the characterisation provided by each rule. A cluster with two positive votes is characterised as malignant. For each rule applied independently the obtained true and false characterizations are shown in Table 2. It is clear that the obtained performance is not acceptable.

The neural network classifier has been used for the initial and the enhanced feature sets. To evaluate the performance of the method we have used two fold cross validation and we performed ROC analysis. For each training set (fold) we have applied the training algorithm ten times with different initial weight values. For the initial feature set A_{zmax}=0.70. The mean A_z is 0.65 and the standard deviation is 0.04. For the enhanced feature set the classification performance is improved remarkably

resulting in A_{zmax}=0.76 with mean A_z 0.71 and standard deviation 0.04. The BCR values was found 0.72 and 0.77 for the original and enhanced feature set. When only the four rule based features constitute the input vector the characterization is poor resulting A_{zmax}=0.72 mean 0.66 and standard deviation 0.05.

Similarly, the SVM classifier has been used with the initial, enhanced and four rule based feature sets. The hyperparameters providing with the best A_z performance of the SVM scheme are: C=25×10^4, ε=0.001 and γ=10^{-6}. In the original feature set the use of PCA was beneficial for the method resulting in $A_z = 0.79$ using 20 and 18 support vectors for malignant and benign, respectively (Fig. 5). In the case of enhanced feature set we have obtained $A_z = 0.77$, while in the case of using only the four rule based features we have obtained $A_z = 0.67$. The BCR values were 0.81 and 0.78 for the original and enhanced feature set, respectively. In contrast to the neural network case the use of the enhanced dataset does not lead to performance improvement.

4 Discussion and conclusions

A methodology for the characterization of microcalcification clusters in digitised mammograms in malignant or benign has been developed. In the final stage of the methodology two major classes of classifiers have been used: neural networks and support vector machines. SVMs using Gaussian kernel function provided with the best performance (classification rate 0.81 and $A_z = 0.79$) for the original feature set, which consists of 33 features.

Comparison of our methodology with other reported in the literature is not straightfoward because experiments were conducted on different datasets. Using human extracted feature characterization A_z=0.89 was reported (BAKER *et al.*, 1995; WU *et al.*, 1993). Manual specification resulted in A_z=0.83 (JIANG *et al.*, 1996a) and A_z=0.89 (CHAN *et al.*, 1998). Experiments with the Nijmegen database are reported in (LEE *et al.*, 2000) where an automated method is presented exhibiting sensitivity 0.77 with specificity 0.90. For the same dataset BCR=0.75 is reported in (VERMA, 1999).

The proposed methodology is fully automated. It is executed in three stages and to our knowledge exhibits better performance compared with other fully automated methods for the Nijmegen database. Its performance can be further improved if the cluster boundaries were more precisely identified. This constitutes a subject for future work.

In our method we have proposed a methodology to extract a new type of features which called rule based features. The addition of such features improves significantly the performance of neural networks but the same does not happen for SVMs. We have also found that the reduction of the dimensionality of the feature vector using PCA was beneficial for both classification methods. Finally, the best performance was achieved with SVMs, which offer the additional advantage that their performance does not depend on parameter initialisation, which is the case for neural network methods.

Although the obtained characterization performance can be considered satisfactory, further studies must be carried out for the evaluation of the system with larger datasets. Also, the use of additional features originating from the image itself, such as cluster location and orientation, and patient data can further improve the diagnostic value of the system. Finally, it will be interesting to experiment with image fusion techniques to combine information obtained from both mammographic views (MLO and CC).

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References

BAKER, J.A., KORNGUTH, P.J., LO, J.Y., WILLIFORD, M.E., and FLOYD, C.E. (1995): 'Breast Cancer: Prediction with Artificial Neural Network Based on BI-RADS Standardized Lexicon', *Radiology*, **196**, pp. 817-822

BATTITI, R. (1992): 'First and second order methods for learning: Between steepest descent and Newton's method', *Neural Computation,* **4**, pp. 141-166

BAZZANI, A., BEVILACQUA, A., BOLLINI, D., BRACACCIO, R., CAMPANINI, R., LANCONELLI, N., RICCARDI, A., ROMANI, D., and ZAMBONI, G. (2000): 'Automated detection of clustered microcalcifications in digital mammograms using an SVM classifier', *Proc Eur Symp on Artificial Neural Networks*, pp. 195-200

BISHOP, C.M. (1996): 'Neural Networks for Pattern Recognition' (Oxford University Press, 1996).

BOTTEMA, M.J., and SLAVOTINEK, J.P. (2000): 'Detection and classification of lobular and DCIS (small cell) microcalcifications in digital mammograms', *Pattern Recognition Letters,* **21**, pp. 1209-1214

BURGES, C.J.C. (1998): 'A Tutorial on Support Vector Machines for Pattern Recognition', *Knowledge Discovery and Data Mining*, **2**, pp. 1-43

CHAN, H.-P., LAM, K.L., PETRICK, N., HELVIE, M.A., GOODSITT, M.M., and ADLER, D.D. (1998): 'Computerized analysis of mammographic microcalcifications in morphological and texture feature space', *Med. Phys.,* **25**, pp. 2007-2019

CHAN, H.-P., LO, S.C.B., SAHINER, B., LAM, K.L., and HELVIE, M.A. (1995): 'Computer-aided detection of mammographic microcalcifications: Pattern recognition with an artificial neural network', *Med. Phys.,* **22**, pp. 1555-1567

CHANG, C.-C., and LIN, C.-J. (2001) 'LIBSVM: Introduction and Benchmarks', [Online], Available: http://www.csie.ntu.edu.tw/~cjlin/libsvm

CHANG, C.-C., and LIN, C.-J. (2002): 'LIBSVM: a Library for Support Vector Machines (version 2.33'), [Online], Available: http://www.csie.ntu.edu.tw/~cjlin/libsvm

CRISTIANINI, N., and SHAWE-TAYLOR, J. (2000): 'An Introduction to Support Vector Machines and other kernel-based learning methods' (Cambridge University Press, 2000)

DENGLER, J., BEHRENS, S., and DESAGE, J.F. (1993): 'Segmentation of microcalcifications in mammograms', *IEEE Trans. Med. Imag.*, **12**, pp. 634-642

EL-NAQA, I., YANG, Y., WERNICK, M.N., GALATSANOS, N.P., and NISHIKAWA, R. (2002): 'Support vector machine learning for the detection of microcalcifications in mammograms', *Proc Int. Con. Image Processing*

GAVRIELIDIS, A., LO, J.Y., VARGAS, R., and FLOYD, C.E. (2000): 'Segmentation of Suspicious Clustered Microcalcifications in Mammograms', *Med. Phys.*, **27**, pp. 13-22

HARA, T., YAMADA, A., FUJITA, H., IWASE, T., and ENDO, T. (2001): 'Automated classification of mammographic microcalcifications by using artificial neural networls and ACR BI-RADS criteria', In: SONKA, M., HANSON K.M., (Eds): Medical Imaging 2001: Image processing, Proc. SPIE, 4322, pp. 1783-1787

JIANG, Y., NISHIKAWA, R.M., METZ, C.E., WOLVERTON, D.E., SCHMIDT, R.A., PAPAIOANNOU, J., and DOI, K. (1996a): 'A Computer-Aided Diagnostic Scheme for Classification of Malignant and Benign Clustered Microcalcifications in Mammograms', *Proc 3rd Inter. Workshop on Digital Mammography, pp.* 219-224

JIANG, Y., NISHIKAWA, R.M., WOLVERTON, D.E., METZ, C.E., GIGER, M.L., SCHMIDT, R.A., VYBORNY, C.J., and DOI, K. (1996b): 'Malignant and benign clustered microcalcifications: automated feature analysis and classification', *Radiology*, **198**, pp. 671-678

JOACHIMS, T. (1998): 'Making large-scale SVM learning practical', In: SCHOLKOPF B., BURGES C.J.C., and Smola A.J. (Eds.), Advances in kernel methods – support vector learning, MIT Press, 1998

KARSSEMEIJER, N. (1993): 'Adaptive noise equalization and recognition of microcalcifications in mammography', *Inter. J. Pattern Recog. Artif. Intel.*, **7**, pp. 1357-1376

KEERTHI, S.S., SHEVADE, S.K., BHATTACHARYYA, C., and MURTHY, K. R. (1999): 'Improvements to Platt's SMO algorithm for SVM Classifier Design' (Tech. Rep., Dept of CSA, IISc, Bangalore, India, 1999)

LANYI, M. (1988): 'Diagnosis and Differential Diagnosis of breast Calcifications' (Spinger-Verlag, 1988)

LEE, S.K., LO, C.S., WANG, C.M., CHUNG, P.C., CHANG, C.I., YANG, C.W., and HSU, P.C. (2000): 'A computer-aided design mammography screening system

for detection and classification of microcalcifications', *Int. J. Med. Informt.*, **60**, pp 29-57

LEFEBVRE, F., BENALI, H., GILLES, R., KAHN, E., and DI PAOLA, R. (1995): 'A fractal approach to the segmentation of microcalcifications in digital mammograms', *Med. Phys.*, **22**, pp. 381-390

LI, H., LIU, K.J.R., and LO, S.C.B. (1997): 'Fractal modelling and segmentation for the enhancement of microcalcifications in digital mammograms', *IEEE Trans. Med. Imag.*, **16**, pp. 785-798

MEERSMAN, D., SCHEUNDERS, P., and VAN DYCK, D. (1998): 'Classification of microcalcifications using texture-based features', In: KARSSEMEIJER N., THIJSSEN M., HENDRIKS J. and VAN ERNING L., (Eds): *Digital Mammography '98*, Nijmegen, Netherlands, pp.233-236

METZ, C.E. (1986): 'ROC methodology in radiologic imaging', *Invest. Radiol.* **21**, pp. 720-733.

NAKAYAMA, R., UCHIYAMA, Y., HATSUKADE, I., YAMAMOTO, K., WATANABE, R., NAMBA, K., KITAGAWA, K., and TAKEDA, K. (1999): 'Discrimination of malignant and benign microcalcification clusters on mammograms', *J Comp Aided Diag Med Imag*, **3**, pp. 1-7

PAPADOPOULOS, A., FOTIADIS, D.I., and LIKAS, A. (2002): 'An automatic microcalcifications detection system based on a hybrid neural network classifier', *Artif Int Med*, **653**, pp. 1-19

PLATT, J. (1998): 'Sequential Minimal Optimization: A fast algorithm for training support vector machines' (Tech. Rep., Microsoft Research, MSR-TR-98-14, 1998)

ROGOVA, G.L., STOMPER, P.C., and KE, C.-C. (1999): 'Microcalcification texture analysis in a hybrid system for computer-aided mammography', In: HANSON K.M., (Eds): Medical Imaging 1999: Image processing, *Proc. SPIE*, **3661**, pp. 1426-1433

SCHMIDT, F., SORANTIN, E., SZEPESVARI, C., GRAIF, E., BECKER, M., MAYER, H., and HARTWAGNER, K. (1999): 'An automatic method for the identification and interpretation of clustered microcalcifications in mammograms', *Phys. Med. Biol.*, **44**, pp. 1231-1243

SHEN, L., RANGYYAN, R.M., and DESAUTELS, J.E.L. (1994): 'Application of shape analysis to mammographic clacifications', *IEEE Trans. Med. Imag.*, **13**, pp. 263-274

STRICKLAND, R.N., and HAHN, H.I. (1996): 'Wavelet transforms for detecting microcalcifications in mammography', *IEEE Trans. Med. Imag.*, **15**, pp. 218-228

SOLTANIAN-ZADEH, H., POURABDOLLAH-NEZHAD, S., and RAFIEE RAD, F. (2001): 'Shape-based and texture-based feature extraction for classification of microcalcifications in mammograms', In: SONKA, M., HANSON K.M., (Eds): Medical Imaging 2001: Image processing, *Proc. SPIE*, **4322**, pp. 301-310

TAYLOR, P., FOX, J., and POKROPEK, A.T. (1999): 'The development and evaluation of CADMIUM: a prototype system to assist in the interpretation of mammograms', *Medical Image Analysis*, **3**, pp. 321-337

VAPNIK, V. (1995): 'The Nature of Statistical Learning Theory' (Spinger, 1995).

VELDKAMP, W., KARSSEMEIJER, N., OTTEN, J.D.M., and HENDRIKS, J.H.C.L. (2000): 'Automated classification of clustered microcalcifications into malignant and benign', *Med. Phys.*, **27**, pp. 2600-2608

VERMA, B.K. (1999): 'Comparative Evaluation of Two Neural Network based Techniques for Classification of Microcalcifications in Digital Mammograms', *Knowleage & Information Systems: An International Journal*, **1**, pp. 107-117

WANG, T.C., and KARAYANNIS, N.B. (1998): 'Detection of microcalcifications in digital mammograms using wavelets', *IEEE Trans. Med. Imag.*, **17**, pp. 498-509

WU, Y., GIGER, M.L., DOI, K., VYBORNY, C.J., SCHMIDT, R.A., and METZ, C.E. (1993): 'Artificial neural networks in mammography: application to decision making in the diagnosis of breast cancer', *Radiology*, **187**, pp. 81-87

YOSHIDA, H., DOI, K., and NISHIKAWA, R.M. (1994): 'Automated detection of clustered microcalcifications in digital mammograms using wavelet transform techniques', In: Loew M.H., (Eds): Medical Imaging 1994: Image processing, *Proc. SPIE*, **2167**, pp. 868-886

YU, S., and GUAN, L. (2000): 'A CAD system for the automated detection of clustered microcalcifications in digitised mammogram films', *IEEE Trans. Med. Imag.*, **19**, pp. 115-126

ZHAO, D., (1993): 'Rule-based morphological feature extraction of microcalcifications in mammograms', In: LOEW M.H., (Eds): Medical Imaging 1993: Image processing, *Proc. SPIE,* **1095**, pp. 702-715

Table 1: Features for cluster categorization.

Microcalcification (MC) cluster classification features	
Area of the cluster convex hull	Mean MCs intensity
Cluster area	Mean perimeter of MCs in cluster
Cluster eccentricity	Minor cluster's axis (equivalent ellipse)
Cluster elongation	Neighbouring with a larger cluster
Cluster Entropy	Number of MCs in cluster
Clusters' equivalent diameter	Orientation of cluster
Extent of cluster	Solidity of cluster
Filled area in cluster	Spreading of MCs in cluster
Major cluster's axis (equivalent ellipse)	STD of distances from cluster centroid
Mean contrast	STD of MC compactness
Mean distance from cluster centroid	STD of MC elongation
Mean local MC background	STD of MC intensity
Mean MC area	STD of MCs area
Mean MC background intensity	STD of MCs contrast in cluster
Mean MC compactness	STD of MCs perimeter in cluster
Mean MC elongation	The length of the cluster convex hull
Mean MCs eccentricity	

Table 2: Performance of the Rule – Based Classifier.

Pairs of features	Malignant (true characterization)	Benign (false characterization)
Mean cluster eccentricity – mean contrast	28	1
Mean local background – mean distance from cluster centroid	44	5
Mean contrast - mean compactness	33	3
Standard deviation of the microcalcification distances from cluster centroid – equivalent diameter of the cluster	41	4

List of figure captions

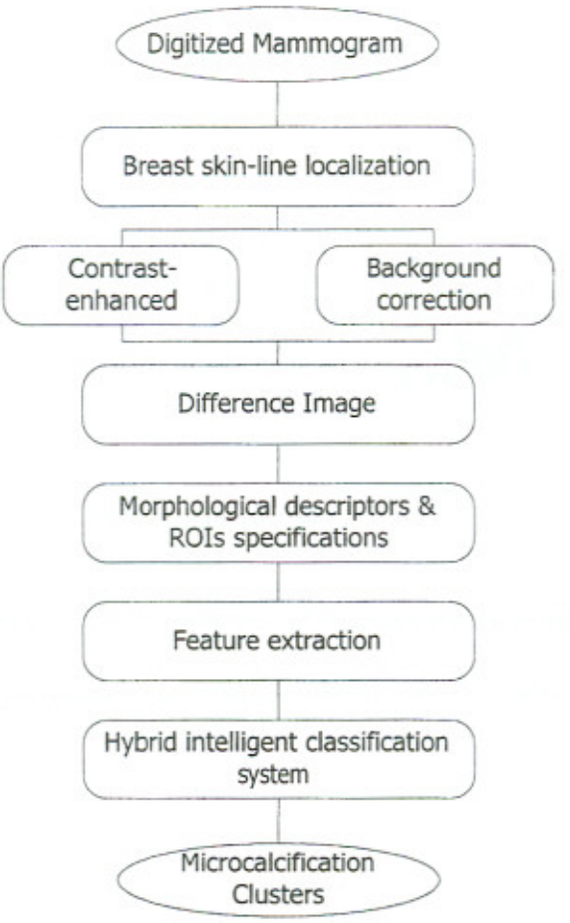

Fig 1. *The microcalcification cluster detection system.*

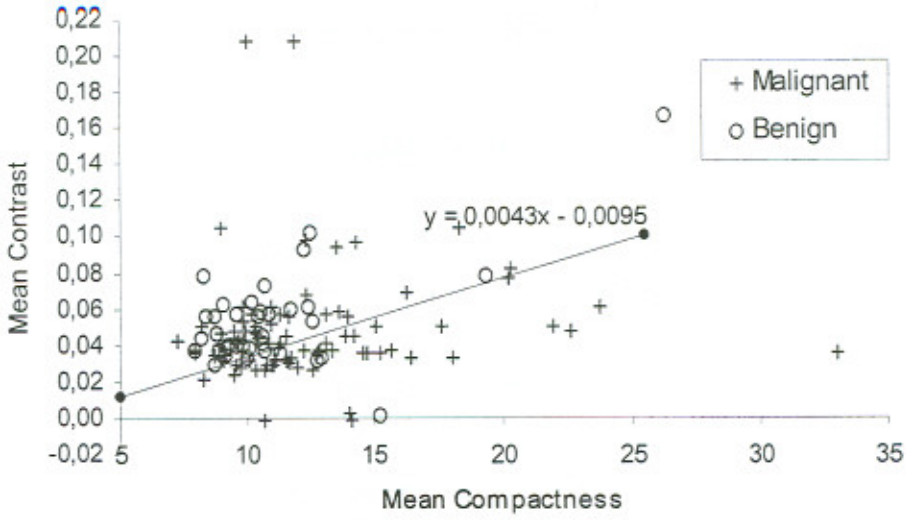

***Fig 2**. Linear decision approximation for the development of rule-extracted features from the 2D plot of mean contrast and mean compactness features in each cluster*

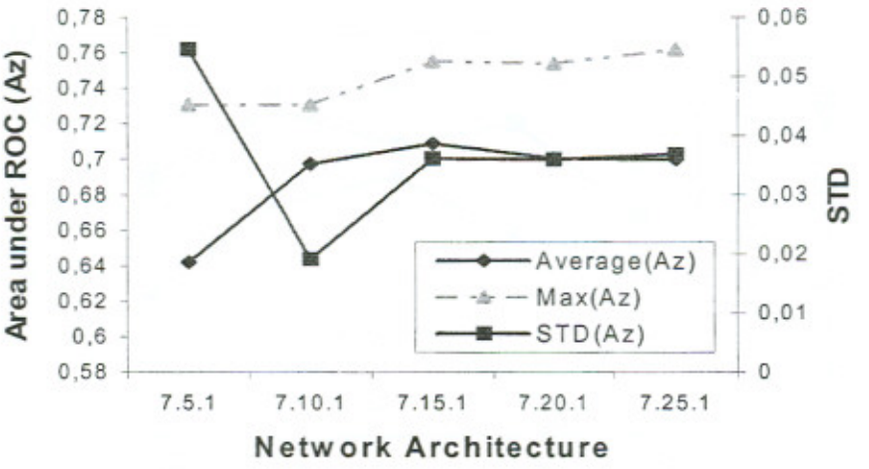

***Fig 3**. The performances of one-hidden layer network architectures for several numbers of hidden nodes*

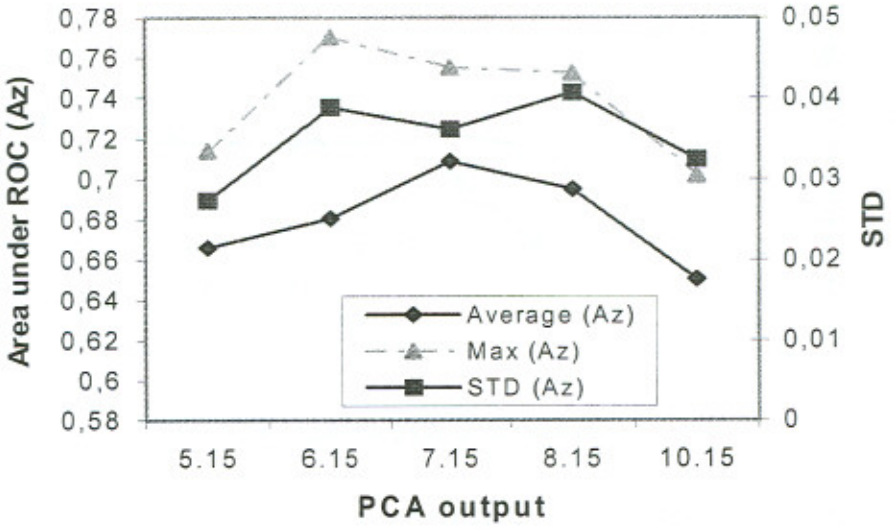

***Fig 4**. The performances of neural networks (one-hidden layer, fifteen nodes) for several PCA outputs are plotted. The maximum, the average and the standard deviation of the Az values are presented for each network.*

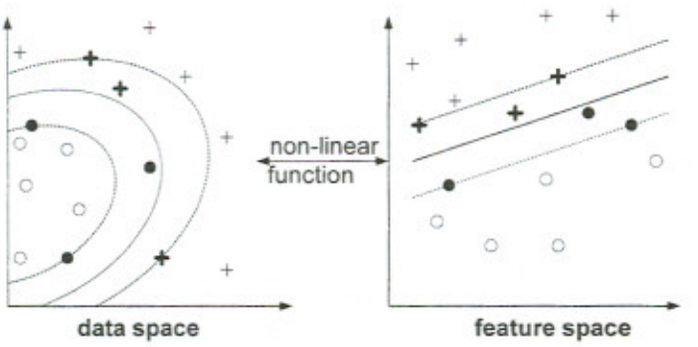

***Fig 5**. A non-linear SVM maps the data from the feature space D to the high dimensional feature space F by the non-linear unction Φ.*

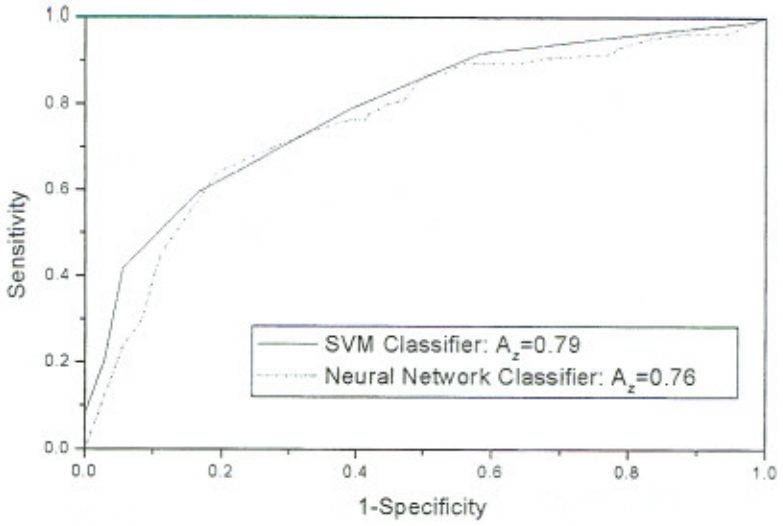

***Fig 6**. The ROC curves of SVM and neural network classifiers (best performance).*