Quantitative analysis of morphological techniques for automatic classification of micro-calcifications in digitized mammograms

C.C. Diaz-Huerta a, E.M. Felipe-Riveron b,⇑, L.M. Montaño-Zetina a

a Research and Higher Studies Center, National Polytechnic Institute, A.P. 14-740, 07000 Mexico City, Mexico
b Centro de Investigación en Computación, Instituto Politécnico Nacional, Av. Juan de Dios Batiz w/n and Miguel Othon de Mendizabal, P.O. 07738, Mexico City, Mexico

Article Info

Article history:
Available online 10 June 2014

Keywords:
Mammogram analysis
Morphological reconstruction
Digital mammography
Micro-calcification detection
Mathematical Morphology

Abstract

In this paper we present an evaluation of four different algorithms based on Mathematical Morphology, to detect the occurrence of individual micro-calcifications in digitized mammogram images from the mini-MIAS database. A morphological algorithm based on contrast enhancement operator followed by extended maxima thresholding retrieved most of micro-calcifications. In order to reduce the number of false positives produced in that stage, a set of features in the spatial, texture and spectral domains was extracted and used as input in a support vector machine (SVM). Results provided by TMVA (Toolkit for Multivariate Analysis) produced the ranking of features that allowed discrimination between real micro-calcifications and normal tissue. An additional parameter, that we called Signal Efficiency/Purity (denoted SE/P), is proposed as a measure of the number of micro-calcifications with the lowest quantity of noise. The SVM with Gaussian kernel was the most suitable for detecting micro-calcifications. Sensitivity was obtained for the three types of breast. For glandular, it detected 137 of 163 (84.0%); for dense tissue, it detected 74 of 85 (87.1%) and for fatty breast, it detected 63 of 71 (88.7%). The overall sensitivity was 85.9%. The system also was tested in normal images, producing an average of false positives per image of 13 in glandular tissue, 11 in dense tissue and 15 in fatty tissue.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

Breast cancer is the most common malignant neoplasm in western women, being the main cause of death in some countries around the world.

Specialists have developed screening programs with the aim of detecting warning signs of cancer, when it is not palpable. One of the main early symptoms is the appearance of small calcium deposits, known as micro-calcifications, whose diameter range from 0.1 to 3 mm. They are seen as bright spots in a mammogram and can be found isolated or forming clusters. Micro-calcifications have been commonly found in women over 50 years old, but recently have been detected in younger women, around 40 years old. In this case, its detection has been more difficult because the glandular breast density is also observed as a bright region in the mammogram, and they could be mistaken in that tissue. In many works, a cluster of micro-calcifications is a group of at least 5 micro-calcifications in a cubic centimeter. Many experts agree that most of them are benign; however, some of them could be malignant and evolve into a carcinoma. Clinical studies revealed that 30–50% of breast cancer cases showed micro-calcifications in mammography images and between 60% and 80% were confirmed by histological examination (Sickles, 1986; Manrique, 1999).

Different methods for automatic detection of micro-calcification clusters in digital or digitized mammograms have been developed in the past (Nishikawa, 2002; Sahiner, Chan, Roubidoux, et al., 2004; Wroblewska, Boninski, Przelaskowski, & Kazubek, 2003). Thangavel, Karnan, Sivakumar, and Mohideen (2005) and Cheng, Cai, Chen, Hu, and Lou (2003) have made an extensive survey of the state-of-the-art on the automatic detection of micro-calcifications in mammograms, which in general follow four steps: first, to reduce the noise and enhance micro-calcifications using image processing techniques; second, to apply a given segmentation technique; third, to extract a group of features of micro-calcifications. Finally, to classify the analyzed objects based on these features in order to determine if the analyzed objects are artifacts or real micro-calcifications.

Due to the many microscopic objects to be identified in a mammogram, there has been the necessity of developing computer algorithms to help physicians to locate them. The creation of an automatic system is intended to provide a “second opinion” in
the detection of micro-calculcations. (Cheng et al., 2003; Mohanalin et al., 2010; Papadopoulos, Fotiadis, & Costaridou, 2008; Zyout, Abdel, & Jacobs, 2009). The most recent advances are focused in developing a Computer-aided detection system for clustered micro-calculcations in reconstructed digital breast tomosynthesis volumes. The algorithm is based on analyzing small volumes that enclose the regions of micro-calculcations. It included morphological methods as region growing and iterative thresholding (Sahiner et al., 2012). Other research is concerned on a knowledge base algorithm, proposed by Oliver et al. (2012). It is based on extracting local features that define the morphology of micro-calculcations. Then a boosting scheme is followed in order to create a strong classifier from the sum of weak classifiers.

There are other approaches mainly focused on the feature selection. The research group of Velayutham and Thangavel (2012) began with a simple processing stage based on histogram equalization and watershed algorithm for segmenting the micro-calculcations. Then, a set of features that included Haralick features, Grey Level Co-occurrence Matrix and some modifications of this matrix (for example Gray Level Difference Matrix-GLDM), and Surrounding Region Dependency Matrix (SRDM) were used. Then, they proposed an unsupervised method for feature selection based on rough set-based entropy measures in order to remove redundant features. They recommended their method when class labels are not known or are incomplete. The method proposed by Yu and Huang (2010) used a wave filter and two thresholds in the stage of image processing. Then a set of textural features based on Markov random field (MRF) and fractal models as well as statistical features were extracted and used as inputs to a BPNN for automatic classification.

Regarding automatic classification of clusters of micro-calculcations, the most common techniques are artificial neural networks (ANN) and support vector machines (SVM). A common problem consisted on the imbalanced distribution of benign and malign instances in the training sets, affecting the performance of classifier. Ren proposed the balanced learning with optimized decision enabling effective learning and then evaluate the performance of both classifiers (Ren, 2012).

The purpose of this work is to analyze the performance of four algorithms reported in the literature for automatic detection of individual micro-calculcations, based on morphological operators. The general procedure in those algorithms consists on the following steps: first, each complete image undergoes a contrast enhancement process in order to highlight micro-calculcations. Then, a thresholding operation is applied, in order to extract size, shape and position of the objects of interest. At this stage, each potential micro-calculcation is compared with those detected by an experienced radiologist, who previously set the ground truth by hand. At this point, sensitivity is compared among the four algorithms and the one with the highest value is selected. After evaluation of sensitivity, a set of features in spatial, texture and spectral domains is obtained, which are inputs to a support vector machine (SVM), in order to filter most of the false positives coming from the processing stage, and with different parameters are finally evaluated in a support vector machine to make an automatic classification of micro-calculcations.

The four algorithms are based on Mathematical Morphology, where the digitized mammogram f is considered as a set of pixels that represents a topographical relief and each pixel is considered as an elevation proportional to its intensity. The dark and light structures of the image correspond to valleys and peaks of this relief, respectively. Some of these peaks correspond to micro-calculcations in mammograms surrounded by background tissue.

Recently, different processing algorithms have been reported in the literature (Betal, Roberts, & Whitehouse, 1997; Dengler, Behrens, & Desaga, 1993; Fu et al., 2005; Halkiotis, Botis, & Rangoussi, 2007; Papadopoulos, Fotiadis, & Likas, 2002; Soille, 2010; Ustymowicz & Nieniewski, 2006). We have implemented them to test their accuracy with different parameter values in order to determine those values that allow the detection of most of the real micro-calculcations.

The paper is organized as follows. Section 2 briefly deals with the materials and methods used in the paper. Section 3 describes the background mainly focused on the morphological operators in which algorithms are based on. Analysis of the algorithms related to the research is included in Section 4. In Section 5 the description of the different types of features to be extracted and evaluated is included. Section 6 explains the support vector machine used for the automatic classification (Diaz-Huerta, Felipe-Riverón, & Montaño-Zetina, 2012). Results and their discussion appear in Section 7 and finally the conclusions are given in Section 8.

2. Materials and methods

Data were obtained from the mini-MIAS database (http://peipa.essex.ac.uk/info/mias.html), which consisted of 322 digitized mammography images owned by the UK National Breast Screening Programme. They were obtained by rescaling MIAS images from 50 to 200 microns pixel size, and consisted of images of 1024 × 1024 pixels with 8 bits per pixel (0 corresponded to black, and 255 corresponded to white). The database provided a diagnosis for each mammogram, giving 23 images with micro-calculcations (benign or malignant). It also provided the coordinates (x, y) at the center of abnormality either in cluster or isolated micro-calculcations and the radius (in pixels) of a circle that contained them. The four algorithms were implemented in MATLAB, using the Image Processing Toolbox morphological functions.

All the mammograms in the mini-MIAS database had labels detailing the orientation and projection of mammography, and notes regarding the patient. We removed that information in the following way: first, we analyzed the gray level in the skin-line region, which was between 14 and 30 (in a scale of 0–255). Pixels with intensity less than 15 were set to zero, because most of them corresponded to the dark region of mammogram and tissue near the surface of the breast. The rest was set to 255, which was associated to breast region, labels and some artifacts related to the X-ray process (lines or bright points due to dust). Then, we applied a morphological opening over this binary image using a disk of radius 30 pixels as a structuring element, in order to separate those labels superimposed to the breast region.

The original breast region was obtained with the process of reconstruction by dilation (Gonzalez & Woods, 2008; Serra, 1982) where the marker f was a black image of size 1024 × 1024 with an isolated white pixel (with gray level 255) at the center, and the mask g was the original image.

The process of reconstruction by dilation, denoted by R δ(f), consists on successive dilations δk(f) of marker image f (black image with isolated pixel) until the propagation of the resulting image is totally limited by the mask image g (original) (Soille, 2010). After this stage, labels were eliminated.

The four image processing algorithms evaluated in this work were applied on each entire image in order to improve the contrast of micro-calculcations over their surrounding and locate those micro-calculcations. Then the segmentation produced a binary image, with white objects associated to potential micro-calculcations.

3. Background

A mammogram f is considered as a set of points arranged in a matrix of size M × N, as described in Section 2. Each mammogram
was probed with a small set $B$, called structuring element, in order to quantify the manner in which it fits within the image. The size and shape of the structuring element should be chosen according to the geometry of the object of interest.

In Mathematical Morphology (Serra, 1982) the two basic operations are erosion and dilation. Erosion is defined as:

$$\delta_B(f)(x,y) = \min \{ f(x+x', y+y') - B(x', y') | (x', y') \in D_B \},$$

where $D_B$ denotes the domain of structuring element $B$. Dilation is defined as:

$$\psi_B(f)(x,y) = \max \{ f(x-x', y-y') + B(x', y') | (x', y') \in D_B \}. $$

Opening and closing are two important operators based on the combination of dilation $\psi_B(f)$ and erosion $\delta_B(f)$ operations. Opening of an image $f$ by a structuring element $B$, denoted by $\gamma_B(f)$ is the erosion of $f$ by $B$, followed by the dilation of the result by reflection of structuring element, denoted by $B^r$:

$$\gamma_B(f) = \psi_B[\delta_B(f)].$$

Similarly, closing of $f$ by $B$, denoted by $\phi_B(f)$ is the dilation followed by erosion. That is,

$$\phi_B(f) = \psi_B[\delta_B(f)].$$

Their combination give rise to White Top Hat (WTH), and Black Top Hat (BTH) operators (Soille, 2010), which are defined, respectively, as:

$$WTH_B(f) = f - \gamma_B(f).$$

$$BTH_B(f) = \phi_B(f) - f.$$

Combination of these operators allows highlighting of bright regions with the Contrast Enhancement operator (Soille, 2010). It is defined as:

$$\kappa_{TH}(f) = f + WTH_B(f) - BTH_B(f).$$

4. Algorithms analysis

In what follows, four processing algorithms are described in detail.

4.1. Algorithm 1: morphological reconstruction and extended maxima segmentation

This classical algorithm was originally proposed by Soille (2010). First, single erosion $\psi^{(1)}_{\epsilon}(f)$ was applied to the entire original image with a disk of a 5 pixels radius as structuring element, removing potential micro-calciﬁcations. The original image was considered as the mask and the eroded image was the marker. The last image is used as the seed for the reconstruction by dilation $R_{\epsilon}$ of the mask. This operation is known as the opening by reconstruction of $f$, defined as:

$$\gamma_{\epsilon}^{(1)}(f) = R_{\epsilon}[\psi^{(1)}_{\epsilon}(f)].$$

This operation included only objects belonging to normal tissue; potential micro-calciﬁcations were retrieved by subtraction of the reconstructed image from the original. This operation, known as White Top-Hat by Reconstruction (RWTH), is defined as $RWTH(f) = f - \gamma^{(1)}_{\epsilon}(f)$.

In our case, $\epsilon = 1$. All micro-calciﬁcations can be considered as peaks, whose heights are associated to gray levels in a scale from 0 to 255, as mentioned in Section 1. After the operation RWTH has been applied these peaks increased their height with respect to their surroundings. However, some artifacts could also increase their heights. In order to filter them, we applied the extended maxima transformation, where only the regional maxima whose heights were higher than $h$ units, remained. The total number of extended maxima can only decrease when increasing the value of $h$. As a result, we got a binary image by choosing an appropriate threshold $h$. Different value of $h$ were tested as thresholds to get binary images. We chose $h$ value in such a way that provided many micro-calciﬁcations as the ground truth.

4.2. Algorithm 2: contrast operator and extended maxima segmentation

This algorithm also was proposed by Soille (2010). In order to filter each micro-calciﬁcation, different structuring elements generally are needed because they have different sizes and forms. An indirect way to implement this task was using the Contrast Enhancement operator $\kappa_{TH}$ described in Section 3.

In order to obtain a binary image the maxima extended transformation used in algorithm 1 was applied. Different thresholding values for $h$ were tested in order to get as many true micro-calciﬁcations as possible. Some large artifacts appeared, due to the union of many small objects after applying this transformation. An analysis done by a specialist showed that most areas of micro-calciﬁcations had less than 30 pixels and only a small amount had areas between 30 and 50 pixels. Taking into account this information, we removed those objects whose areas were greater than 55 pixels.

4.3. Algorithm 3: bicubic interpolation and segmentation by histogram

Part of this algorithm was proposed by Papadopoulos et al. (2002) and used by Hanmandlu, Vineel, Madasu, and Vaskarla (2008). Each entire image $f$ was split in 32 sub-regions. It produced sub-images of size $32 \times 32$ that provided information about the gray level of clustered micro-calciﬁcations (where they exist) and the surrounding tissue. For each sub-image a histogram of gray levels was constructed; it was observed that micro-calciﬁcations fell in the top 30%. The remaining 70% was associated to normal tissue.

For each sub-region the mean gray level of pixels in the lower region was calculated. Results were put in a $32 \times 32$ matrix, and interpolated using bicubic interpolation. The resulting image represented the mean level of the local background, which is denoted as $f_{\text{bg}}$.

To retrieve probable micro-calciﬁcations, the interpolated image $f_{\text{micro}}$ was subtracted from the original $f$. That is,

$$f_{\text{micro}} = f - f_{\text{bg}}.$$ 

Then, segmentation was done in two parallel thresholding processes:

1. Local thresholding. This was done by splitting $f_{\text{micro}}$ in $32 \times 32$ sub-regions, and then identifying pixels with positive values for each region. A defined percentage of them with the highest gray level values was used, producing a binary image ($f_1$). Different percentage values were tested, in order to get as many micro-calciﬁcations as the ground truth provided. $f_1$ contained pixels with high gray level values in comparison with their local neighborhood.

2. Global thresholding. We modiﬁed this part of the original algorithm in order to improve contrast. We applied the White Top-Hat Operator (WTH) to the original image $f$, with a disk of radius 3 pixels as structuring element, instead of the processing used in (Papadopoulos et al., 2002). A defined percentage of pixels with the highest gray level values was
used, producing a second binary image \( f_2 \) associated to the highest gray level values. Different percentage values were tested, as in local thresholding stage.

The output of this algorithm was an image produced by the intersection, \( f_1 \) AND \( f_2 \). It contained real micro-calcifications and a large amount of isolated pixels belonging to normal tissue, according to the diagnosis done by the specialist. These pixels were eliminated.

### 4.4. Algorithm 4: bicubic interpolation and extended maxima segmentation

This algorithm was modified from the third one, in the sense that it combined the processing stage described in Section 4.3 and thresholding by extended maxima (Soille, 2010), used in Section 4.1. We were interested in determining how the sensitivity was modified when a specific morphological transformation was applied.

The procedure started with the image \( f_{micro} \) obtained in Section 4.3. Then, both local and global thresholdings were applied as follow:

1. **Local thresholding.** This was done by splitting \( f_{micro} \) in 32 × 32 sub-regions. Each block was thresholded with the maxima extended transformation, producing a binary image \( f_1 \).

2. **Global thresholding.** After applying the White Top-Hat Operator (WTH) to the original image \( f \), as described in Section 4.3, the maxima extended transformation was used, producing a binary image \( f_2 \).

Finally, the AND operation of \( f_1 \) and \( f_2 \) was done. We tested different threshold values for \( h \) in \( f_1 \) and \( f_2 \), respectively. An additional step consisted on eliminating objects whose area was greater than 55 pixels.

Results of the four algorithms were evaluated using ground truth information, established by a specialist. He determined the location of the centroid of each micro-calcification, taking into account the diagnosis provided by mini-MIAS. He also included or eliminated those objects considered as true micro-calcifications or normal tissue according to his experience.

The algorithm that provided the higher number of true positives was selected as the most suitable processing method. Then a set of features was extracted from both enhanced and binary images produced by the algorithm, in order to reduce the number of false positives, as described in Section 5.

### 5. Feature extraction

After enhancement and segmentation for the most suitable processing algorithm, we extracted a set of 65 features for potential micro-calcifications. These features are described in Tables 1 and 2.

#### 5.1. Spatial domain features

These features are shown in Table 1 for each object in the binary image. Note that features f1 and f17 are the same (the area in pixels) so intentionally established for the purpose of proving the effectiveness of the method used in automatic classification to establish the rank (importance) of the features, as will be explained in Section 7.

Another group of spatial features was computed in small blocks of size 17 × 17 pixels, corresponding to the size of micro-calcifications and normal tissue, as explained in Section 5.3. Each block is centered on the centroid of the potential micro-calcification and two new features were obtained, named average pixel intensity and average energy of the pixel intensity (Zheng, Qian, & Clarke, 1996), which are defined as:

\[
avg = \frac{1}{M \times N} \sum_{m=1}^{M} \sum_{n=1}^{N} f(m, n),
\]

\[
eavg = \frac{1}{M \times N} \sum_{m=1}^{M} \sum_{n=1}^{N} (f(m, n))^2.
\]

The pixel intensity variance (feature f62) is obtained as:

\[
i \var = \sum_{m=1}^{M} \sum_{n=1}^{N} [f(m, n) - avg]^2,
\]

and the energy variance (feature f63) is obtained as:

\[
e \var = \sum_{m=1}^{M} \sum_{n=1}^{N} [f(m, n) - eavg]^2.
\]

#### 5.2. Texture features

Textural properties are based on the Gray Level Co-occurrence matrices defined by Haralick, Shanmugam, and Distein (1973). These matrices measure the relative frequency of occurrence \( P_{ij} \) of two neighboring pixels with intensities \( i \) and \( j \), respectively, separated a distance \( d \), depending on the direction of interest. They are built from information of a small block of size 17 × 17 pixels centered on the centroid of each potential micro-calcification. For each angle between adjacent pixels \( 0^\circ, 45^\circ, 90^\circ \) and \( 135^\circ \) and a distance \( d = 1 \), a set of 11 features is obtained, as shown in Table 2. Features f18 to f28 correspond to \( 0^\circ \); f29 to f39, to \( 45^\circ \); f40 to f50, to \( 90^\circ \) and f51 to f61 correspond to \( 135^\circ \). The total number of textural features is 44.

#### 5.3. Spectral domain

Spectral domain features involve the concept of alternating current energy (AC energy), used in the past for signals and images (Mester & Franke, 1992; Zheng, Qian, & Clarke, 1996)(Table 2). Energy is computed as the sum of squares of de AC spectral coefficients \( c(i,j) \) in a small region of size \( M \times N \), and the block activity \( A \) (feature f64) is obtained as:

\[
A = \sum_{i=1}^{M} \sum_{j=1}^{N} |c(i,j)|.
\]

The most common transform used in block activity is the discrete cosine transform (DCT) because most of the significant information is concentrated in a few coefficients. This feature is a

<table>
<thead>
<tr>
<th>Feature no.</th>
<th>Name</th>
<th>Feature no.</th>
<th>Name</th>
<th>Feature no.</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Area</td>
<td>5</td>
<td>Orientation</td>
<td>15</td>
<td>Compactness</td>
</tr>
<tr>
<td>2</td>
<td>Eccentricity</td>
<td>6</td>
<td>Solidity</td>
<td>16</td>
<td>Elongation</td>
</tr>
<tr>
<td>3</td>
<td>Major axis length</td>
<td>7</td>
<td>Perimeter</td>
<td>17</td>
<td>Area</td>
</tr>
<tr>
<td>4</td>
<td>Minor axis length</td>
<td>8–14</td>
<td>Seven invariant moments of Hu</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
measure of contrast in each block. We used blocks of size $17 \times 17$ corresponding to the size of micro-calcifications and normal tissue.

In turn, spectral entropy (feature f65) is defined as:

$$E = -\sum_{i=1}^{M} \sum_{j=1}^{N} a(i,j) \ln(a(i,j)),$$

where

$$a(i,j) = \frac{|c(i,j)|}{A}.$$

6. Support vector machine for automatic classification

A Support Vector Machine (SVM) is a useful tool to distinguish between true micro-calcifications and normal tissue using only a minimal subset of all training vectors (support vectors). These vectors are composed by the features of each segmented object obtained previously.

Suppose we give a training set of $L$ observations, consisting of a vector of $n$ features $x_i \in \mathbb{R}^n$, $i = 1, \ldots, L$ and an associated truth provided by a reliable source, which is a class label $y_i \in \{-1, +1\}$. The label $+1$ corresponds to real micro-calcifications—and -1 to normal tissue.

The simplest assumption is that data can be separated by the hyperplane:

$$\mathbf{w} \cdot \mathbf{x} + b = 0,$$

where $\mathbf{w}$ is a vector perpendicular to the hyperplane. Each training data is at one side of the hyperplane, according to its class, and is described by:

$$y_i (\mathbf{w} \cdot \mathbf{x} + b) - 1 > 0 \forall i = 1, \ldots, L.$$

The margin is the distance between the support vectors and the hyperplane, and is obtained as $\frac{1}{||\mathbf{w}||}$.

When data are not linearly separable the problem could be solved introducing non-negative slack variables $\xi_i$, $i = 1, \ldots, L$, $\{\xi_i = 0$ if the vector is properly classified; otherwise $\xi_i$ is the distance to the decision hyperplane). The problem is reduced to find parameters $\mathbf{w}$, $b$ and $\xi_i$ that minimizes the cost function:

$$\frac{1}{2} \mathbf{w}^T \mathbf{w} + C \sum_{i=1}^{L} \xi_i,$$

with the following modified restriction:

$$y_i (\mathbf{w}^T \phi(\mathbf{x}_i) + b) \geq 1 - \xi_i, \quad \xi_i \geq 0.$$

The parameter $C$ establishes a trade-off between margin and missclassification.

The extension to nonlinear SVM is performed by mapping the training vectors, $\mathbf{x}_i$ into a higher dimensional feature space. Then SVM finds a linear separating hyperplane with the maximal margin in this higher dimensional space, but considering a kernel function, that eliminates the explicit transformation to the feature space. The three kernels studied in this work were linear, polynomial and radial basis function (Gaussian), which are defined, respectively, as:

$$K(\mathbf{x}, \mathbf{x}_i) = \mathbf{x}_i^T \mathbf{x},$$

$$K(\mathbf{x}, \mathbf{x}_i) = (\mathbf{x}_i^T \mathbf{x} + \theta)^p,$$

$$K(\mathbf{x}, \mathbf{x}_i) = \exp(-||\mathbf{x} - \mathbf{x}_i||^2/2\sigma^2),$$

where $\theta$, $\sigma$ and $p$ are kernel parameters.

7. Results and discussion

A specialist located the coordinates of the centroid of 354 micro-calcifications in 23 images provided by the mini-MIAS database.

Table 3 included parameters of thresholding, as well as the rate of true positives (sensitivity), calculated as the ratio of the number of micro-calcifications detected (true positives TP) and the total of real micro-calcifications manually detected (positives P). It also included the number of false positives (number of objects which are not real micro-calcifications) for each algorithm. It also included some advantages and disadvantages of each algorithm. According to this table, algorithm 3 produced the lowest number of micro-calcifications. Notice that increasing the number of control parameters, the sensitivity decreases. Comparing thresholding methods in algorithms 3 and 4, we conclude that maxima extended transformation produced a higher number of true positives.

Algorithms 1 and 2 used only one control parameter, which resulted in higher sensitivity than algorithms 3 and 4. However, algorithm 1 did not retrieve the exact shape and size of micro-calcifications. Finally, algorithm 2 retrieved most of the micro-calcifications diagnosed by the specialist, keeping the morphology of micro-calcifications, becoming the most suitable in detection after the processing stage.

Results of the processing stage provide advantages and disadvantages of each processing algorithm, as well as the reasons to use a specific one, based on the number of true-positives detected, the number of parameters involved and the type of breast. Detection of each micro-calcification plays an important role in clustering. Specialists agree that clusters formed by at least 4 micro-calcifications per cubic centimeter could evolve into carcinoma. We intended retrieve most of them in order to obtain a cluster with the individual lesions. Many authors have used a specific processing algorithm and then detect the clusters (Mannrige, 1999; Cheng et al., 2003; Halkiotis et al., 2007; Papadopoulos et al., 2008; Wroblewska et al., 2003). In this work, we detected most of the individual micro-calcifications in the stage of processing, thereby reducing the possibility of failing to detect a cluster.

The next step consisted in reduce even more the number of false positives that appeared in the stage of processing. They are part of the connective tissue and ducts due to its small size in image and appear with several micro-calcifications grouped as a...
Table 3
Sensitivity and false positives detected per algorithm for different parameter values. Total number of micro-calcifications: 354.

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Parameter type</th>
<th>Parameter value</th>
<th>True Positives</th>
<th>Sensitivity (TP/P)</th>
<th>False positives</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Maxima extended h</td>
<td>2.5</td>
<td>344</td>
<td>0.9718</td>
<td>1811</td>
<td>(a)</td>
</tr>
<tr>
<td>2</td>
<td>Maxima extended h</td>
<td>6</td>
<td>346</td>
<td>0.9774</td>
<td>2144</td>
<td>(b)</td>
</tr>
<tr>
<td>3</td>
<td>(c)</td>
<td>5%; 5%</td>
<td>257</td>
<td>0.7260</td>
<td>1041</td>
<td>(d)</td>
</tr>
<tr>
<td>4</td>
<td>(e)</td>
<td>2.5; 2.5</td>
<td>335</td>
<td>0.9463</td>
<td>1870</td>
<td>(f)</td>
</tr>
<tr>
<td>5</td>
<td>(f)</td>
<td>2.5; 5</td>
<td>314</td>
<td>0.8870</td>
<td>673</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>5; 5</td>
<td>296</td>
<td>0.8362</td>
<td>325</td>
<td></td>
</tr>
</tbody>
</table>

(a) Segmentation did not produce the size neither the shape of the original.
(b) Distinguish between two closely micro-calcifications.
(c) Percentage of pixels for Local threshold pctlloc. Global threshold pctlglob.
(d) Not appropriate for detection in dense-glandular breast.
(e) Global extended maxima hglob; Local extended maxima hloc.
(f) More parameters in segmentation process than in algorithms 1 and 2.

classified as background and the total of background; signal purity (SP) is the ratio of the objects well detected as signal and the total of objects classified as signal and background; the product of signal efficiency and signal purity (SE*P) is a measure of the highest quantity of signal with the lowest quantity of noise; significance (Sig) is the ratio of the number of instances well detected as signal and the Poisson error associated to detection.

TMVA provided a suitable cut value for output of SVM, which corresponded to the maximum value of significance (Sig), and gave specific values for the rest of the parameters (SE, BE, SE*P and SP). Notice that maxima values for both Sig and SE*P corresponded to the same cut value.

ROC area and sensitivity are the main parameters reported in literature that measure performance of an automatic detection system (Thangavel et al., 2005). We propose an additional parameter, known as Signal Efficiency-Purity (SE*P) as another measure of performance in classification. This parameter has not been proposed in the literature so far as it is considered in this paper.

Fig. 1(b) shows an example of behavior of ROC area (AUC) of three kernels for default values of TMVA, for 60 features. According to ROC area the most suitable classifier is linear, followed by Gaussian and finally the polynomial.

Fig. 2 shows the behavior of ROC area, SE and SE*P for Gaussian, linear and polynomial kernel. The cut point for the suitable number of features corresponded to the highest values of the three parameters, from which Fig. 2c produced 60 features for Gaussian (Fig. 2a), 15 and 45 for linear (Fig. 2b) and 50 for polynomial. Both the ROC area and the SE*P increases as the number of features increases. SE did not show a specific tendency. Notice in Fig. 2b an overtraining zone for linear kernel considering 20, 25 and 30 features; by increasing the number of features does not increase the signal efficiency, but it decreases.

Table 5 shows that for linear SVM, the lower the number of features (15 for the linear kernel), the lower both SE*P and the ROC area. Meanwhile, SE is random. However the same number of features for different SVM kernels produced similar results (see Gauss σ = 10 and polynomial).

Quantitative evaluation of processing algorithms followed by a selection of the most suitable algorithm to use in the automatic classification, provided results that are comparable to those reported in (Fu et al., 2005). The highest ROC area in this study
was 0.976, which corresponded to Gaussian kernel, followed by polynomial kernel, with 0.972, as shown in Table 5.

We selected the support vector machine with Gaussian kernel and sigma = 100 to determine the sensitivity and specificity in detection of micro-calcifications in the 22 images, and in 45 normal images of different type of tissue. For images with micro-calcifications, the overall sensitivity was 85.9% ± 4.0% at a confidence level of 95%. The overall specificity was 89.2% ± 1.0% at a confidence level of 95%.

These measurements were also obtained in a separate way for three types of breast considered in the mini-MIAS database, as shown in Table 6. Notice that fatty breast had the highest sensitivity (88.7%), but also the highest average false positive per image in mammograms with micro-calcifications as well as in normal images. In second place, for dense breast, the sensitivity was 87.1%. Notice that for this kind of tissue, the specificity and the average false positives per image for the two kinds of images (normal and abnormal) had the minimum value. Finally, the algorithm produced the minimum value for sensitivity in glandular tissue (84.0%), but the same value than fatty tissue. The average false positive per image was higher than dense but lower than fatty breast.

Normal images used in this work were randomly selected, and checked by the specialist, in order to determine if they did not contain any micro-calcification. Some objects found by the support vector machine were considered as potential lesions, in the sense that the specialist considered them as possible real micro-calcifications. Some of them were false positives. The medical practice suggested in doubt cases is the biopsy, for histological corroboration.

The sensitivity of detection system depends on the database and the type of detection [Rizzi, D’Aloia, & Castagnolo, 2012]. Many researches use mammograms obtained from local health centers and some others use mini-MIAS or DDSM databases. Some of them focus in detecting ROI’s of clustered micro-calcifications or individual calcifications, and comparisons of different detection systems are difficult for this reason. For example, (Scaranello, Crystal, Bukhanov, & Helbich, 2010) reported 71 of 74 (96%) malignant micro-calcifications using a commercially available CAD system (Second Look version 7.2, iCAD, Inc.). On the other hand, (Yang, Liu, & Zhai, 2012) obtained 125 of 128 (97.1%) of calcification cancers using the same system. Finally, (Zyout et al., 2009) obtained a sensitivity of 91.3% with his approach of Bayesian algorithm.

The overall sensitivity of this work in detecting individual micro-calcifications was 85.9% ± 4.0%.

There are other works that are devoted to diagnose breast cancer using a set of features obtained from the Wisconsin Breast Cancer Dataset (WBCD) based on measurements of a biopsy from human breast cancer tissue and a SVM classifier. The classification accuracy was 99.51% (Fatih, 2009). The main difference between these methods is the type of features. WBCD have a dataset of pathological measurements in cancerous cells, which are used as features to feed a SVM.
8. Conclusions

Micro-calcifications are non-palpable lesions that appear in mammograms and could evolve into a carcinoma. Many countries around the world have implemented screening programs with the purpose of detecting early symptoms. The most advanced countries produce digital mammograms, but the rest produce analog mammograms, which could be digitized. The main disadvantage of digitized mammograms is the loss of quality in the image. It depends on the original image and the resolution of the digitizer. However, the mini-MIAS database has been used for many years as a standard for research in detection of micro-calcifications and is a reference when different algorithms are compared.

Automatic detection of micro-calcifications is a support for radiologist, working as a “second opinion”, pointing to those lesions that could be not clear in a mammogram. This work provided additional information to the mini-MIAS database, about the size and position of all micro-calcifications.

We have presented a quantitative evaluation of four algorithms of processing digitized mammograms mainly based on Mathematical Morphology in order to detect most of the potential micro-calcifications. After thresholding stage in each algorithm we obtained sensitivity that allowed us to know how many real micro-calcifications are located in each image, providing information about what algorithm is the most suitable to use before filtering noise with the support vector machine. The algorithm based on...
contrast enhancement and thresholding with extended maxima produced most of the potential micro-calculcations.

This work relates the concepts of signal and background usually used in High Energy Physics with true micro-calculcation and background tissue (or noise) usually found in mammography and relate the concepts of significance and signal efficiency-purity with micro-calculcation detection. It provided the higher quantity of micro-calculcations with the lower quantity of background, which corresponded to normal tissue. We evaluated performance of support vector machine (SVM) for linear, Gaussian and polynomial kernels, testing variations of cost parameter C, kernel parameters and number of features. Gaussian kernel gave the best result for ROC area. We used this SVM to analyze mammograms of dense, glandular and fatty tissue. The algorithm of detection used in this work had the better sensitivity for fatty breast tissue.

The main disadvantage of the database used in this work is the resolution and the quality of the image. Since the pixel size is 200 μm, our algorithms cannot detect micro-calculcations smaller than this size. Besides, images too clear or too dark could hide true micro-calculcations.

In this work we are detecting individual micro-calculcations of different size and shape, and other algorithms detect clusters of micro-calculcations or ROIs that include clusters. Therefore, it is difficult to compare results of different algorithms.

Other contribution of this work is the relation between the concepts in detection of particles in High Energy Physics and detection of micro-calculcations in mammograms, as well as the behavior of signal efficiency and ROC area when varying the kernel type, the number of features and the cost parameter.

The next step in this research will consider clustering these isolated micro-calculcations detected with this approach, using textual properties and classify them as benign or malign clusters using support vector machines. In addition, we will work with other mammographic databases that provide digital images, in order to test the performance of the algorithms and compare them with other detection approaches.

Acknowledgements

The authors would like to thank Secretaría de Investigación y Posgrado, Centro de Investigación en Computación (CIC) of the Instituto Politécnico Nacional (IPN), Instituto de Ciencia y Tecnología del Distrito Federal (ICyT-DF) and also Consejo Nacional de Ciencia y Tecnología (CONACyT) and Sistema Nacional de Investigadores (SNI), Mexico, for their economic support to this research.

References

1559–1568.