A System for Computer Aided Early Diagnosis of Breast Cancer based on Microcalcifications Analysis

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Abstract:
We propose that a system for medical diagnosis, in order to be reliable and useful, beyond systematic evaluation must follow also some basic guidelines: (a) it must be designed as open and self-explanatory giving the opportunity to the physician to understand the method and the rules comprised in the system, (b) it must be properly designed to provide maximum effectiveness in physician's diagnosis instead of being fully automated aiming solely in its own maximum effectiveness of diagnosis, (c) it must be easily adapted to the physician's expertise through interactive feedback. The main aim must be the optimization in physician's diagnosis through the use of the system instead of the optimization of system's diagnosis alone. We present a system for computer aided early diagnosis of breast cancer that is physician oriented instead of being fully automated. Clustered microcalcifications have been considered as important indicators of the presence of breast cancer. The system is at present based on the detection and analysis of these objects in order to help the physician in the early diagnosis of breast cancer. The basic concepts of the proposed system are: (a) optimized visual examination of certain cancer indices, (b) critical feature quantification and classification, (c) adaptation to doctor's expertise through interactive feedback, (d) real time explanation of the suggested diagnosis flowchart, (e) patient oriented monitoring of clinical data. The performance of the system has been evaluated through laboratory tests on digitized and annotated mammograms from the Nijmegen Digital Mammogram Database as well as on mammograms from the well documented archive of mammographic images of "Prolipsis" Diagnostic Breast Center.

Keywords:
Biology and medicine, Computer–aided diagnosis, Breast Cancer

1. Introduction

Breast cancer is the most common cancer type among women, and the second leading cause of death in women after lung cancer [Zhou (1989)]. Years of experience have revealed that mammography constitutes the most efficient method in the early diagnosis of this type of cancer. Between 30 to 50 % of the infraclinic cases [Vyborny (1994)] are discovered by the presence of microcalcifications on the mammographic films. The microcalcifications are deposits of calcium salts, i.e. galactic, tricalcium phospates, that are either benign (intra-galactophoric or intra-tissular) or malignant [Bassett (1992)]. Usually they appear in the form of clusters and are easy to distinguish on the films due to their high density.
Several efforts have been made to classify the microcalcifications in benign and malignant according to their characteristics. Among the most known are these of Le Gal [Le Gal (1976), (1984) – Fondrinier (2002)] and Lanyi [Lanyi (1977), (1985)]. Other studies performed use Computer-Aided Design (CAD) Mammography [Fam (1988), Davies (1990), Kegelmeyer (1994), Lee (2000)]. The most known methods of Computer Aided Design Mammography are the artificial neural networks (ANN) with automatic classifiers [Wu (1992), (1993), Zhang (1994), (1996), Chan (1995), Gurcan (2002)], the segmentation method [Dengler (1993), Gavrielides (2002)], wavelets [Lado (2001)] or, shape, size and multiscale analysis [Shen (1994), Laine (1994), Buchbinder(2002)] to distinguish between malignant and benign cases.

We present an approach in the classification of microcalcifications with a system that is physician oriented and capable to be adapted to the physician's expertise through interactive feedback. It is based on detailed examination of microcalcification and cluster features as measured with the aid of experienced radiologists. Each microcalcification is examined individually and the predefined characteristics are calculated. In addition, some cluster features such as the cluster polymorphism, the number of high risk microcalcifications and a cluster risk index, are provided. Also, the influence of cluster position and direction as well as patient's history and age may be taken into account for the final estimation of the risk. The whole project is accomplished in three levels that include: a) patient archiving, b) use of image analysis tools for image examination and finally c) the detection and classification of the existing microcalcifications.
Preliminary results of the system's evaluation based on data from biopsies demonstrate the ability of the system to correctly encouraging or discouraging biopsy. The current limitations of the system as well as the future work on this project are discussed.

2. Materials and Methods

2.1 The Workstation Configuration

The workstation of "Hippocrates-MST" comprises of any modern PC with sufficient memory, processing power and storage capability for high resolution image handling (Recommended: at least 512 MB RAM, Pentium IV 2GHz, 80GB Hard Disk at 7200 RPM), accompanied with a modern CD-Recorder, a proper monitor, a high quality film scanner and, optionally, a laser printer. The film scanner must have optical resolution of at least 300 dpi (Recommended: 600 dpi), wide optical density range (Recommended: 0.0 to at least 3.5 O.D.), at least 12-bit output, quick scan rate (Recommended: at least 100 lines/sec) and minimum scanning area greater than 18 cm x 24 cm. A schematic of such a workstation is shown in Figure 1.

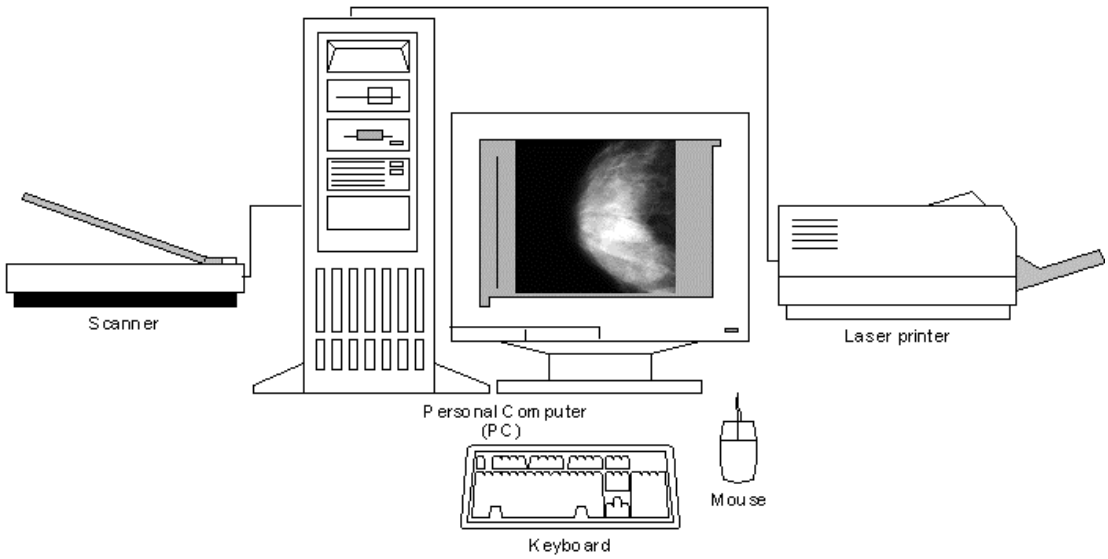

Figure 1. A schematic of "Hippocrates – MST" workstation.

2.2 Detection of Microcalcifications

The detection of microcalcifications is implemented through an algorithm based on the following major steps:

(a) High – Pass Filtering
(b) Variance Normalization
(c) Adaptive Filtering

The algorithm has been developed in accordance to the flowchart shown in Figure 2. When the digital mammographic image is loaded, the user may select either a suspicious region of interest, or the whole image for processing. We use unsharp masking image processing techniques. The image, or selected portions, is first extensively smoothed by using median filtering, and subsequently the resulting image is subtracted from the original. Consequently, large–scale features in the original image are subtracted out, leaving behind an enhanced version for small–scale features. Afterwards, in order to improve the filtering, variance normalization is used, adjusted by fitting a plot of variance versus the median signal level in local areas. The noise model, which is fitted to the data, has the form:

$$\text{noise} = \frac{\sqrt{\dfrac{1}{1/m^2 + 1/d^2} + r^2}}{s} \qquad (1)$$

where m is the median image value, d is the saturation level (the intensity at which an increase in image brightness produces no further increase in intensity value), r is an additive noise term and s is a scale factor. The unsharp mask image is divided by this noise model to create an image, where the value of each pixel is a measure of the significance of the pixel as compared to the local median. The next and final step in the image processing is the application of an adaptive filter [12]. The adaptive filter smoothes regions where there are no statistically significant data values above a given threshold, but applies little or no smoothing to regions where significant values are found.

What remains after the steps of unsharp masking, variance normalization and adaptive filtering is an image showing small–scale structures, which exceed a given threshold compared to the local mean, and the threshold is consistent throughout the image. Moreover, the intensity of an object in the processed image corresponds directly to its statistical significance compared to the local background.

2.3 Image Segmentation and Feature Extraction

The image produced from the unsharp masking image processing technique is subject to threshold segmentation. The threshold is defined each time by an algorithm responsible for optimum threshold searching. A binary image is then produced, clearly demonstrating the revealed objects. This image may undergo a despeckling procedure in order to avoid single pixel noise and afterwards the microcalcifications may obtain their initial gray scale color through a proper image fusion technique.

The user may select a region of interest (i.e. a cluster of microcalcifications) and subsequently the program calculates 7 features for each calcification: (i) existence of dark center, (ii) size, (iii) brightness, (iv) irregularity, (v) circularity, (vi) branching, (vii) circumvolution.

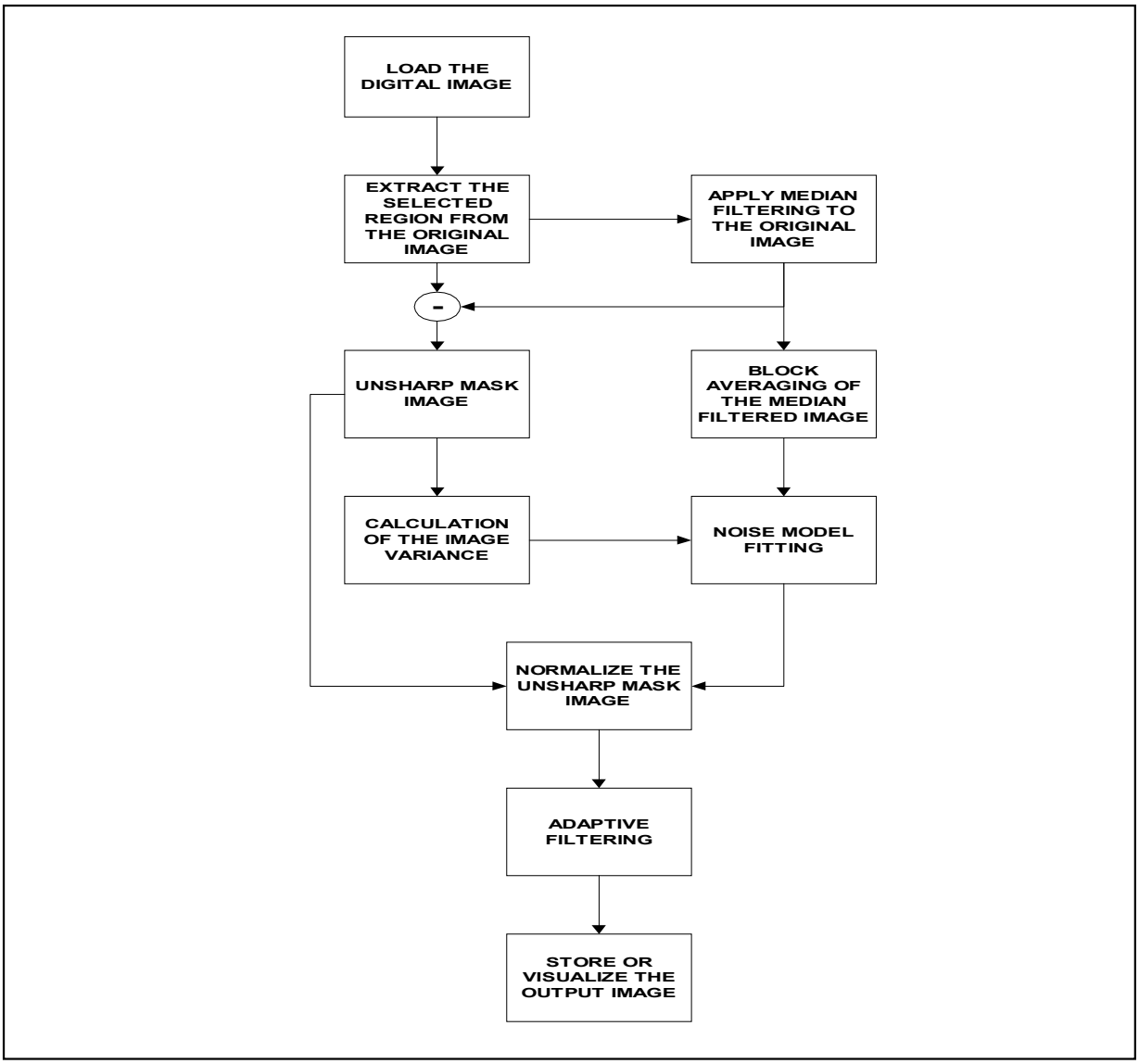

Figure 2. The flowchart of the algorithm responsible for the detection of microcalcifications

2.4 Classification of Microcalcifications and Final Diagnosis

Each microcalcification is assigned with an estimated risk, according to the values of the previously mentioned seven features, based on a flowchart built on experts' rules. The risk distribution of the microcalcifications is then produced and several related parameters such as number of microcalcifications on very high risk, mean risk etc, are calculated. These parameters along with the calculation of polymorphism drive to the classification of the cluster.

The system has been made to be adaptive to expert's opinion; therefore the medical expert may observe the distribution of each feature and modify the related threshold. Thus, the medical expert is able to adjust the criteria used by the program, in order to get it closer to a reliable diagnosis. In addition to this, the medical expert is able to decide whether the position and direction of the cluster along with the age and history of the patient have to be included in the diagnosis model and with what grade of influence.

The final diagnosis is characterized by an estimation of the risk of the suspect microcalcifications cluster. Four virtual zones of risk have been considered:

- **Zone 1** with risk between 0 % and 35 % (definitely benign : it discourages biopsy)
- **Zone 2** with risk between 35 % and 55 % (benign with doubts : it encourages biopsy)
- **Zone 3** with risk between 55 % and 70 % (malignant with doubts : it encourages biopsy)

- **Zone 4** with risk between 70 % and 100 % (definitely malignant : it encourages biopsy)

2.5 Evaluation Procedure

Our developed image processing algorithms succeed in revealing existing microcalcifications from the noisy and low contrast background of mammograms. An initial evaluation of the detection algorithms' performance has been completed, using the Nijmegen Digital Mammograms Database, which contains digital mammograms with annotated benign and malignant clusters of microcalcifications.

As far as the evaluation of the classification algorithm performance is concerned, 71 mammograms containing microcalcifications have been used from the well documented archive of "Prolipsis" diagnostic breast center. These 71 mammograms contain 74 clusters of microcalcifications inside areas that have undergone biopsy and thus there is histological verification of their status. The default cluster risk estimation has been written down, and it has been classified into the above four zones of risk.

3. Results

Among the 74 clusters of microcalcifications, there have been 22 malignant cases, 47 benign cases and 5 cases of atypia. The distribution of the estimated risk for the malignant cases is shown in Figure 3, as well the corresponding distribution for the benign cases is shown in Figure 4. As far as the five cases of atypia are concerned, the estimated risk was calculated between 55% and 70%, i.e. inside the **Zone 3**.

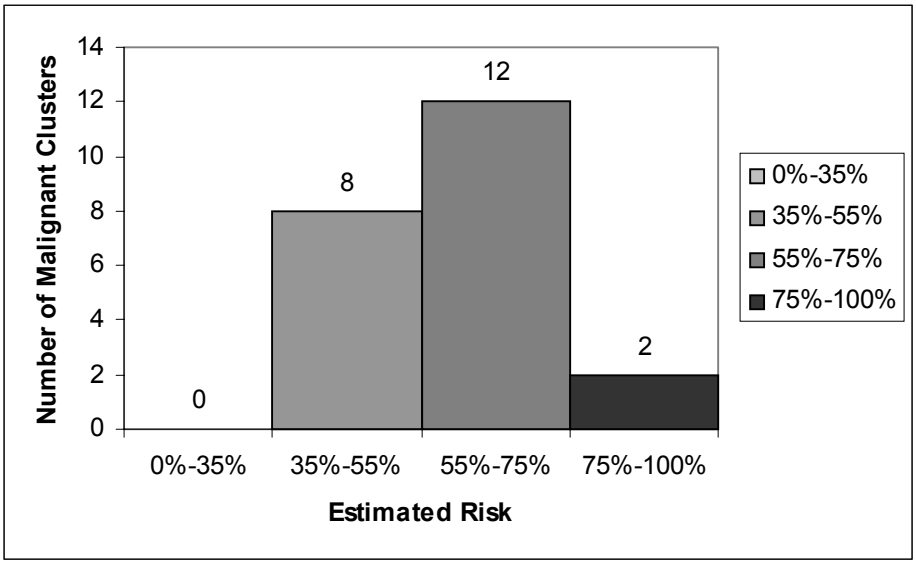

Figure 3. The distribution of the estimated risk for the malignant cases

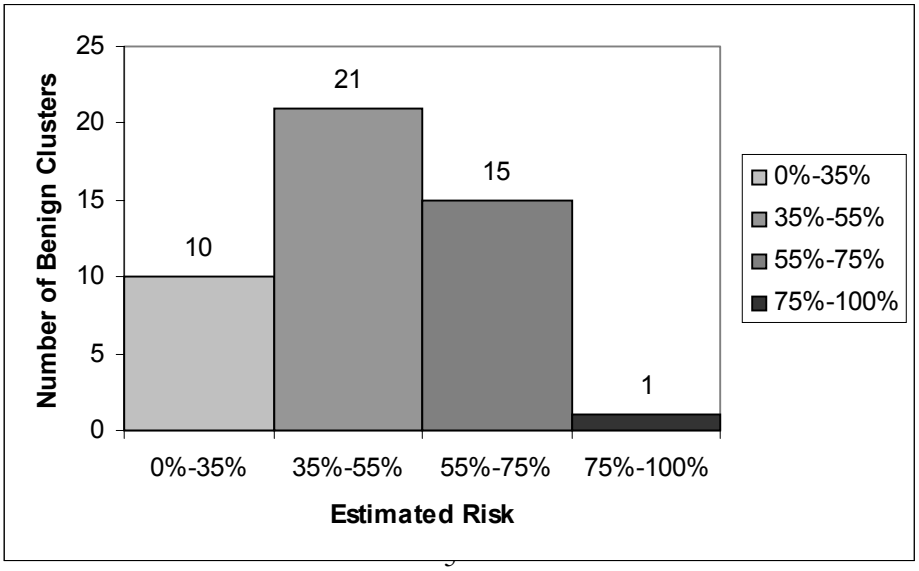

Figure 4. The distribution of the estimated risk for the benign cases

5. Conclusions

As far as the malignant cases are concerned, the system would encourage biopsy to all of them. That is, there is not any false negative as far as the encouragement for biopsy is concerned. For the benign cases, the system would not send for biopsy 10 out of 47 cases. In other words, it would be able to achieve a reduction of 21.28 % on the unnecessary biopsies. There are also 37 false positive (as far as the encouragement for biopsy is concerned). Furthermore, the system demonstrates stable behavior to the cases of atypia, giving them a risk inside **Zone 3** (malignant with doubts: it encourages biopsy), which is also the approach of medical experts in such cases.

It is conceivable that the system estimates the risk of breast cancer towards the right direction. However, although it presents high sensitivity, it suffers from relatively low specificity. This indicates that there is an overestimation of risk driven from the attempt to minimize the false negative results. However, there is the need for a better compromise which will emerge after a fine tuning in the calculation of parameters and the setup of thresholds concerning the selected features of the microcalcifications and their clusters.

6. Acknowledgements

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7. References

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