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Clinical Trial of a CAD System for Microcalcification Detection and Classification

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Abstract

According to the World Health Organisation, breast cancer is the second leading cause of cancer deaths in women today and is the most common cancer among women, excluding nonmelanoma skin cancers. Several studies have proved that the early detection of breast cancer can reduce mortality rates and improve the chances that the patient is diagnosed at an early stage and treated successfully. Mammography is widely used as the primary method for breast cancer detection.

Breast microcalcifications usually appear in the form of clusters and sometimes can be easily detected on mammografic films due to their high clustering density. An approach in the classification of microcalcifications has been presented by Ligomenides et al. and it is based on detailed analysis and evaluation of seven features of individual microcalcifications and of formed clusters. The proposed system is now in clinical trial in an Athens University Hospital's Breast Unit. The results from the first 51 cases (all biopsy tested) that were processed are presented in this paper and indicate that all malignant cases were classified correctly.

Keywords:

computer aided diagnosis, mammogram, microcalcifications, breast cancer, clinical trial

Introduction

Breast cancer is the second leading cause of cancer deaths in women and is the most common cancer among women, excluding nonmelanoma skin cancers. According to the World Health Organization, more than 1.2 million people will be diagnosed with breast cancer every year worldwide. The chance of developing invasive breast cancer during a woman's lifetime is approximately 1 in 7 (13.4%). The death rates from breast cancer also declined significantly during the last years, with the largest decreases among younger women. This is attributed to earlier detection and more effective treatments.

Breast microcalcifications are considered a very useful index of malignancy, which helps in the early detection of breast cancer. Malignant calcifications may occur with or without the presence of a tumor mass and are typically clustered, varying in size and shape. Mammography is accepted as the most effective method to detect breast cancer. However, interpreting a mammogram is not easy for not experienced radiologists. The aim of computer aided detection techniques in breast cancer is to improve the chance that a malignant region is detected and appropriately evaluated. It is very important for the success of the treatment that any malignant area is detected as early as possible. Furthermore, the ability to discriminate benign cases (specificity) is a major issue in computer-aided diagnosis.

Breast microcalcifications are viewed as bright spots with diameter varying from 0.1 to 0.3 mm and usually appear in the form of clusters that can be detected on mammographic films due to their high clustering density. Nevertheless, the existence of microcalcifications in breast tissue is not always a clear evidence of malignancy. Many research efforts have been made to segment medical image findings and specifically to classify breast microcalcifications as benign or malignant, based on computer-aided analysis of their structural and photometric characteristics as those appear in mammographic images.

A computer aided diagnosis (CAD) system, called Hippocrates-mst, has been developed and is based on detailed analysis and evaluation of related features of individual microcalcifications and of formed clusters. The output of the system is considered to be very useful to the radiologists, giving them extra input before reviewing each case.

After an initial evaluation that was done in the laboratory with a set of 200 mammograms, the system is now been tested in a Breast Unit of an Athens University Hospital. The system's integration and ease of use within the unit's workflow as well as the results are examined closely as they may indicate future developments.

Methods

Microcalcification detection and analysis is carried out with the use of an algorithm based on the processing of

three image data sets: a) the application of a high pass filter b) the variance normalization c) the application of an adaptive filter. Similar techniques have been successfully used to process medical and astronomical images.

The proposed methodology for microcalcification classification uses a four-way projection method and examines each microcalcification cluster from four different viewing angles in order to process all possible variations of each view. Seven characteristics are extracted for each microcalcification including size, circularity, existence of sub dense center, brightness level, anomaly of shape, existence of apophyses and branches and existence of windings.

The workstation of the system comprises of a modern IBM compatible personal computer, a printer and a high quality film scanner unless a digital mammographic device exists.

Each case is processed as follows: each mammogram has to be digitized using certain parameters and then the doctor/user enters the patient's demographic data and medical history in the system's digital patient record. After those initial steps the doctor has the option to examine the mammogram(s) using the provided digital tools. These tools include modules as the 'digital lens', which helps users to zoom in an area of interest, or the brightness, contrast and -value adjustment tools that help the user reveal anomalies in a selected area of the mammogram. At the next step, the doctor can use the system's microcalcification detection algorithms and reveal the microcalcifications of a selected area. The microcalcifications of this area are counted and categorized using a color-based categorization.

The final results of the Hippocrates-mst system are presented in a risk percentage scale from 0 to 100. Percentage lesser than or equal to 35 means there are not enough evidence to support sending the patient for a biopsy test. Percentage from 35 to 55 declares benign state and a biopsy test is suggested, while percentage greater than 55 indicates malignancy and a biopsy test has to be made as soon as possible. It must be stated that the system only makes suggestions to the doctor and it is the doctor that makes the final decision whether a case has to be sent for a biopsy test or not.

As from February 2006 the Hippocrates-mst system is used on a daily basis in the Hippocratio Hospital Breast Unit. The Breast Unit belongs to the 1st Propaedeutic Surgical Clinic of the University of Athens Medical School and is fully equipped with: Mammography system (Siemens Mammomat 3000 Nova), Ultrasound system (Siemens Sonoline), Fischer's Table, Vacuum assisted Breast Biopsy (Mammotome), and Ductal endoscopy.

Hippocrates-mst is used following a specific clinical evaluation protocol. Our goal, in this initial clinical trial phase that will last for 6 months, is to achieve integration within the Breast Unit's workflow and make sure every case that would be Mammotome examined would also be processed with the CAD system. During this initial phase of the clinical trial protocol, the system's results must be compared versus the corresponding biopsy results.

The clinical workflow of a typical case involving Hippocrates-mst is as follows: the woman/patient undergoes breast clinical examination along with a mammographic examination. Depending on the mammogram and the clinical examination results, there are a number of options. In case the mammogram shows signs of suspicious microcalcifications or in case there are findings suggesting malignancy, the patient undergoes a Mammotome examination.

When a case is processed with Hippocrates-mst CAD system, the doctor (usually one of the Unit's radiologists) selects the mammogram(s) that must be digitized and scans it/them using the system's scanner. Then adds the resulted image files to the patient's digital record and begins to process each mammogram using Hippocrates-mst's digital image tools and classification modules. At the final step of the computer-aided examination, the system provides the doctor with the overall risk estimation for the selected region of interest. After reviewing a case, the doctor has the option to save the results, along with any notes on the case, to the system's hard disk drive or to a cd. The whole process from the film digitization to the final results takes no more than 6 minutes.

The sample images set contained 51 mammograms, of both craniocaudal and mediolateral views, with microcalcifications collected in a period of five months, from March 2006 to mid July 2006. Each case was accompanied with the patient's demographic data and medical history as well. Indications for mammography could be routine check up, screening or follow-up.

The mammoraphic images obtained through digitization using UMAX 1000XL scanner, with a resolution of 300 dots per inch (DPI), 16 bit greyscale colour depth and .tiff unzipped as the image format. The image size for each image was 2048X2048 while the size in megabytes was approximately 10 MB for each image.

Results

So far 51 cases have been reviewed and biopsy tested, following the clinical trial workflow mentioned earlier.

It must be stated that all these cases would have gone either to surgery or biopsy using Mammotome so every successful indication of a benign case from the CAD system would save this woman from an unnecessary surgery or biopsy.

The initial results have shown that 17 out of 51 patients that underwent biopsy with Mammotome had an actual -

tissue biopsy proven- malignant finding. The system successfully identified all malignant cases showing no false negatives. Furthermore, regarding the benign cases, Hippocrates-mst was able to identify that eighteen of them were benign or possibly benign assigning them a percentage between 0 and 55.

Discussion

The clinical trial protocol worked flawlessly as there were no problems in the CAD system's integration in the Breast Unit's workflow. The doctors were tutored on how to use the system and were able to quickly review each case using Hippocrates-mst's digital image tools as well as the microcalcification detection and classification module.

The laboratory's as well as the first clinical evaluation test results of all malignant cases were encouraging, since no malignant cases were falsely classified as benign. It must be stated here that the correct categorisation of malignant cases was our primary goal during the proposed system's development.