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FALSE POSITIVE REDUCTION IN COMPUTER AIDED DETECTION OF MAMMOGRAPHIC MASSES USING CANONICAL CORRELATION ANALYSIS

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ABSTRACT

X-ray mammography is the most widely used modality for screening breast cancer in the early stages. Computer aided detection (CADe) systems intend to help radiologists in improving the detection rate. However, the drawback of CADe systems is that they result in a high false positive rate (FPR). In this paper, a new feature-fusion-based system is proposed for classifying automatically detected masses in a mammogram as true masses or false positive cases. In this system, unilateral and bilateral information is fused using a multivariate statistical technique called canonical correlation analysis (CCA). The proposed system is validated using a public database called the mammographic image analysis society (MIAS) database. When compared to unilateral, bilateral and conventional-fusion based systems, the overall classification performance of the proposed system is higher by a range of 8%-16%, 12%-16% and 14%-28% in terms of accuracy, area under curve (AUC) and equal error rate (EER), respectively. Further, the reduction in FPR for the proposed system is at least 39%, 35% and 33% at true positive rates (TPRs) of 60%, 65% and 70%, respectively.

Keywords: *Biomedical Image Processing, Cancer Detection, Decision Support System, False Positive Reduction, Mammography.*

1. INTRODUCTION

Breast cancer is the primary cause of death in women. To prevent morbidity and mortality due to breast cancer, early detection and diagnosis becomes necessary. A mammogram which is a low-dose X-ray image of the breast can depict the earliest sign of breast cancer even in asymptomatic woman. While the goal of screening mammography is to detect abnormal breast changes in women before any signs are noticeable, diagnostic mammography aims in evaluating the abnormalities, *i.e.*, to determine the probability of malignancy. It has been shown that screening mammography in particular can reduce breast cancer mortality rates [1].

In mammography, the absorption of the X-rays and hence the image formation depends on density. Breast cancers are radiodense, i.e., they appear white on mammograms. Hence fatty tissue that is radiolucent and appears dark gray-to-black on mammograms provides a good background to visualize cancer. As the density of the breast tissue increases, interpretation of mammograms becomes difficult [2]. The fact that a mammogram is a 2-D projection of the compressed breast causes some limitations especially in dense cases. One of the limitations is that the superimposition of normal breast tissue might simulate a suspicious lesion. This leads to unnecessary biopsies that cause physical, emotional and financial discomfort to the patient. Biopsy is an invasive procedure which is considered to be the gold standard to determine whether a tumor is malignant. About 65-85% of biopsy operations are reported to be unnecessary. The other common problem is that abnormalities might be obscured by the overlapping glandular tissue. Missed malignancies result in a delayed treatment and severe implications including loss of life. It has been reported that radiologists fail to detect 10-30% of cancers. Early and subtle cancers could add to the problem. So also are factors that include fatigue and oversight of the radiologists [3], [4].

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A computer aided detection/diagnostic system (CAD) can be used to aid radiologists in interpreting mammograms. Many studies show that the use of a CAD system as a second reader has the potential to improve the accuracy of breast cancer detection and diagnosis. Computer aided detection (CADe) systems determine suspicious regions called regions of interest (ROIs) in the breast images. However, due to the complex nature of mammograms, CADe systems suffer from a high number of false positives. False positives are normal regions misinterpreted as suspicious ROIs. The second stage of a CADe system following detection of suspicious regions is false positive reduction. This is achieved by classifying the detected ROIs as normal tissue or abnormal. Computer aided diagnostic systems (CADx) systems classify the abnormal regions as benign or malignant [3], [5].

Radiologists usually search for visual indicators on a mammogram for detection and diagnosis of breast cancer. A mass is an important and the most common indicator of breast cancer. Masses appear as dense regions on mammograms. High false positive rate (FPR) is especially a problem in the detection of breast masses, due to the similarity between normal parenchymal structures and masses [6].

While analyzing mammograms, radiologists normally rely on multiple sources of information to improve the detection and diagnostic performance. A common practice of the radiologists is to not only analyze the mammogram under consideration but also do a combined analysis of the image and its contralateral counterpart to evaluate abnormalities. The former involving a single image is called unilateral analysis and the latter that involves the right and left mammogram pair (bilateral mammograms) is called bilateral analysis. An increased density observed in unilateral analysis usually increases the suspicion that the ROI is abnormal, though the region can also be a normal dense tissue. However, as the parenchymal distribution in the right and left breasts are usually symmetric for normal cases, asymmetric densities are an indicative of abnormality [7], [8].

In developing a CADe system for breast cancer detection, combining unilateral and bilateral information would serve to mimic the radiologist's practice of combining these two information sources for assessing mammograms. This work focuses on developing a new fusion algorithm for false positive reduction in the computer aided detection of masses.

Various researchers have addressed the problem of false positive reduction using unilateral analysis. This involves direct characterization of ROIs in terms of features which would be helpful in distinguishing a false positive from a true positive, *i.e.*, a mass. The use of texture features for distinguishing masses from false positives has been widely employed. Khuzi et al. [9] proposed the use of gray level co-occurrence matrix (GLCM)-based texture features to distinguish masses from false positives. Llado et al. [10] employed local binary patterns (LBP) to represent the texture of ROIs for their classification. Masotti et al. [6] suggested the use of gray-scale invariant ranklet texture features for false positive reduction in detection of breast masses. Li et al. [11] used morphological features for elimination of false positives. Tourassi et al. [12] employed a template matching technique with mutual information as the similarity metric for false positive reduction.

Bilateral image analysis has also been explored by researchers for false positive reduction. The idea behind bilateral analysis is that an ROI which is not symmetric with respect to its contralateral counterpart is possibly abnormal. Bovis et al. [13] extracted GLCM features from bilateral difference images for ROI classification. Wu et al. [8] developed a CADe system in an attempt to exploit the advantages of unilateral analysis and bilateral analysis for false positive reduction. Here, unilateral and bilateral (GLCM texture and morphological) features are used to train two different classifiers. The resulting unilateral and bilateral scores respectively, are fused at the decision level to obtain a final score which decides whether the suspicious ROIs are masses or false positives.

Normally, feature fusion is effective when the features across the modalities to be combined are correlated. Decision fusion can be useful if the information provided by the different modalities is complementary in nature. However, when the modalities to be combined provide a mixture of correlated and uncorrelated features, it cannot be concluded as to which of these two techniques is better [14]. Recently, canonical correlation analysis (CCA) [15] which is a multivariate statistical technique is finding increased use in determining associations among features for pattern recognition.

In this work, CCA followed by feature fusion is employed to combine the unilateral and

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bilateral features so as to improve the classification performance in false positive reduction. The rest of the paper is organized as follows; in section 2, the proposed method is discussed. Section 3 presents the results and discussion. Finally, section 4 concludes the work.

2. PROPOSED METHOD

In this work, the mammographic image analysis society (MIAS) database is used [16]. The dataset used to validate the proposed algorithm consists of a total of 86 ROIs automatically segmented from different mammogram images from the MIAS database, where 45 ROIs are normal cases, i.e., false positives and 41 ROIs are masses, i.e., true positives. The block diagram of the proposed system is illustrated in Figure 1.

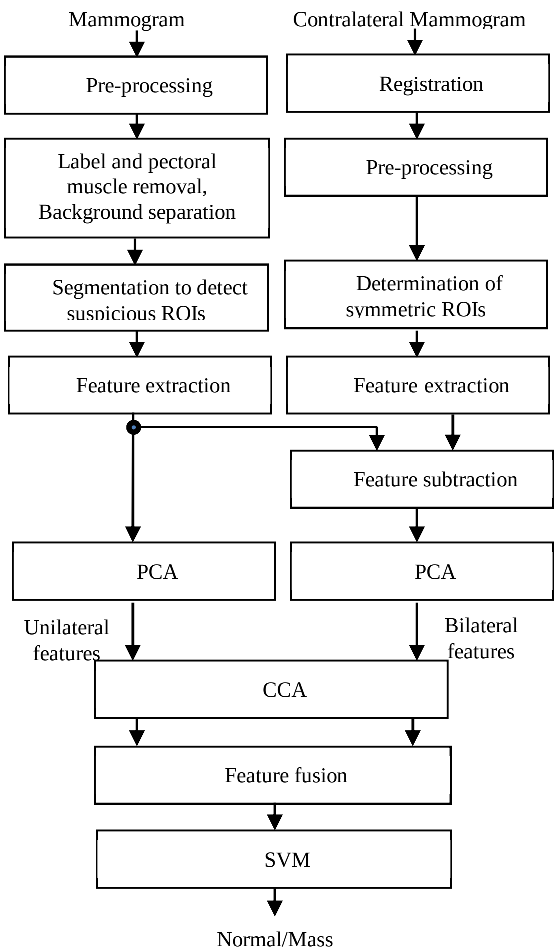

Figure 1 Block Diagram Of The Proposed System

2.1 Unilateral Analysis

In unilateral analysis, information is derived only from the mammogram under consideration. Here, features are extracted from suspicious ROIs of unilateral images. These features are a representative of the characteristics of the suspicious ROIs, which will serve to distinguish between false positives and true positives, *i.e.*, the masses.

First the mammogram to be analyzed is subjected to a series of pre-processing steps. Two-dimensional (2D) median filtering using a 3×3 mask is first applied on the images for removing noise. This is followed by contrast limited adaptive histogram equalization (CLAHE) for image enhancement [17]. Prior to segmentation for detection of masses, radio-opaque artifacts such as labels have to be removed from the mammogram. This is mainly due to their high intensity on the mammogram which will affect the segmentation process. For removing the labels, global thresholding is performed. Following this, morphological opening is performed on the resulting binary image using the area of the largest object. Then the breast profile is separated from the background by performing a series of morphological operations. These morphological steps serve to refine the border between the breast and the background and also to remove any possible holes in the binary image. Refinement of the breast boundary removes isolated pixels and noise near the boundary. After background separation, the pectoral muscle is removed from the mammogram as it is also a high density structure. For pectoral muscle, seeded region growing technique is applied [18].

Following these steps, an adaptive thresholding algorithm based on multi-resolution analysis is employed to perform segmentation. The method employs a two-level wavelet transform (Daubechies DB10) for analyzing the image at different resolutions. A combination of histogram-based global thresholding and adaptive local thresholding is applied on the multi-resolution images to detect the suspicious regions [19].

Figure 2(a) shows a mammogram image (mdb013) from the MIAS database in which the mass is encircled. The segmented output is shown in Figure 2(b) in which the ROI corresponding to the mass has been enclosed by a circle and that corresponding to false positive is enclosed by a rectangle. A total of 14 Haralick's texture features [20] computed from GLCM are then extracted from the suspicious ROIs of the mammogram being analyzed. These features represent the unilateral features.

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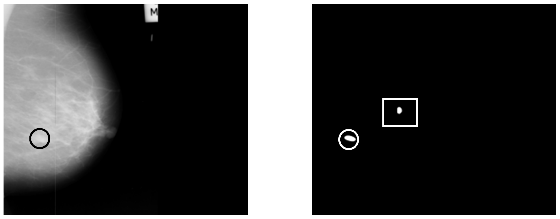

Figure 2 (A) A Sample Mammogram (Mdb013) From MIAS Database (B) Segmented Output

2.2 Bilateral Analysis

Bilateral features are those derived from both the mammogram under consideration and its contralateral counterpart. The idea behind bilateral analysis is that if an ROI is a false positive, the contralateral ROI will have same characteristics as the former due to natural symmetry of the two breasts. Instead, if the ROI is a mass, then there will be a large deviation between the contralateral ROIs. In the bilateral analysis, features are extracted from the contralateral ROI also and following this, difference features are obtained. Thus the bilateral features which are computed by finding the difference between the features of ROIs of the two mammograms is useful for classifying the given ROI.

The most important and non-trivial step in bilateral analysis is registration of the mammogram being analyzed with the contralateral mammogram. This is performed to compensate for the spatial variations in bilateral mammograms and hence necessary for comparing corresponding points of the left and right breasts. Possible sources of variations in the two breasts include differences in positioning of the breasts and the amount of pressure applied to them during image acquisition [21]. In this work, the mammogram image to be analyzed is the reference image and the contralateral mammogram which is the target image is registered to the former. For performing registration, three corresponding control points are identified on the bilateral mammograms [22]. These include the nipple point and two corner points between the chest wall and the breast boundary. Using these control points, the optimal affine transformation which determines the best mapping between the bilateral mammograms is determined [23].

In Figure 3(a), the contralateral mammogram (mdb014) corresponding to the mammogram in Figure 2(a) is shown. Figure 3(b) shows the registered contralateral mammogram. Following registration, the contralateral mammogram is subjected to median filtering for noise removal and CLAHE for enhancement. To obtain bilateral features, the 14 Haralick's texture features are first extracted from symmetric ROIs in the contralateral mammogram. Following this, difference between these features and the corresponding unilateral features is determined. These difference features represent the bilateral features.

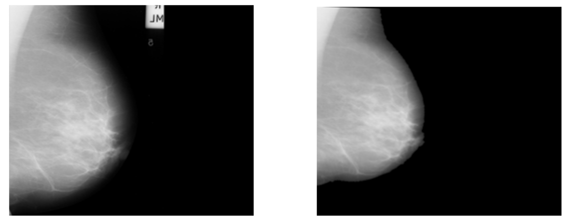

Figure 3 (A) Contralateral Mammogram (Mdb014) (B) Registered Contralateral Mammogram

2.2 CCA-Based Feature Fusion

For combining information from the unilateral features and bilateral features, principal component analysis (PCA) is first employed on the two feature sets individually. PCA is effective in removing noise and redundancy in the data and has been used in many applications including mammogram analysis for dimensionality reduction [24]. Following this, CCA is applied on the two datasets. CCA is a rotation transformation, which when applied to two multivariate sets maximizes the correlation between them and thus makes them more informative when they are fused at the feature-level.

CCA seeks optimal directions U_1 and U_2 respectively, in which two multivariate datasets X_1 and X_2 are maximally correlated. To determine these directions, CCA solves the maximization problem in Equation (1).

$$\max_{U_1,U_2}\{corr[Y_1,Y_2]\} = \max_{U_1,U_2} \frac{U_2^T R_{12} U_1}{\sqrt{U_1^T R_{11} U_1}\sqrt{U_2^T R_{22} U_2}} \qquad (1)$$

where Y_1 and Y_2 are the transformed canonical variates. R_{11} and R_{22} are the autocorrelation matrices of X_1 and X_2, respectively and R_{21} is the cross correlation matrix of (R_1, R_2). Equation (1) can be formulated as a Lagrangian optimization problem which in turn is specified in Equation (2).

$$\max_{U_1,U_2} U_2^T R_{12} U_1$$

subject to

$$U_1^T R_{11} U_1 = U_2^T R_{22} U_2 = 1 \qquad (2)$$

which results in the Lagrangian equation,

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$$L(U_1, U_2, \alpha, \beta) = U_2^T R_{21} U_1 - \frac{\alpha}{2}(U_1^T R_{11} U_1 - 1) - \frac{\beta}{2}(U_2^T R_{22} U_2 - 1) \quad (3)$$

Solving Equation (3) yields the optimal canonical projections U_1 and U_2. The CCA transformed feature sets are then subjected to feature fusion. Feature fusion is performed using the concatenation strategy which is widely employed [15]. The fused feature vector is then used to train a support vector machine (SVM) with radial basis function (RBF) kernel for false positive reduction. SVM classifier with RBF kernel has been shown to be effective for breast cancer diagnosis [25]. A nested two-level, 10-fold cross validation strategy is used for model selection and performance evaluation.

3. RESULTS AND DISCUSSION

The performance of the proposed system is compared with the unilateral system, bilateral system and feature fusion without CCA (concatenation of raw features). Further, the proposed scheme is also compared with popular decision fusion schemes. These include two hard decision strategies, i.e., the *OR* fusion and the *AND* fusion and a soft decision fusion scheme called the linear weighted sum rule [14]. The weights used in the linear weighted sum fusion are determined using the validation accuracy weighting scheme [26]. For all these systems, PCA is used for reducing the dimensions of the raw features. The optimum number of dimensions retained in all the systems is determined in the model selection phase.

In Table 1, the accuracy, area under curve (AUC) and equal error rate (EER) of various systems have been compared. It is observed from Table 1 that proposed scheme outperforms all the other schemes in terms of all the three performance measures. The improvement achieved by the proposed system in terms of accuracy, AUC and EER when compared to the unilateral system is 10%, 16% and 14% respectively. It can also be observed that the proposed system outperforms the bilateral system by 14%, 16% and 28% in terms of these parameters. Among the conventional fusion schemes for combining unilateral and bilateral information, the *OR* logic based decision fusion performs the best. The performance gain achieved by the proposed system when compared to this system is 8% in accuracy, 11% in AUC and 14% in EER.

Table 1: Comparison Of Accuracy, AUC And EER Of Various Systems

System		Accuracy (%)	AUC	EER
Unilateral		67.53	0.6726	0.3333
Bilateral		65.15	0.6726	0.4000
Feature Fusion		67.53	0.6968	0.3556
Decision Fusion	*AND*	63.95	0.6982	0.3556
	OR	68.60	0.7004	0.3333
	Linear weighted sum rule	66.28	0.6947	0.3333
CCA-based feature fusion (Proposed)		**74.42**	**0.7817**	**0.2859**

For further analysis, the unilateral system, bilateral system, *OR* decision fusion (best among conventional fusion schemes) and the proposed system are considered. The receiver operating characteristic (ROC) plots of these systems are presented in Figure 4. It can be observed that the ROC plot of the proposed system is more close to ideal than the rest of the systems.

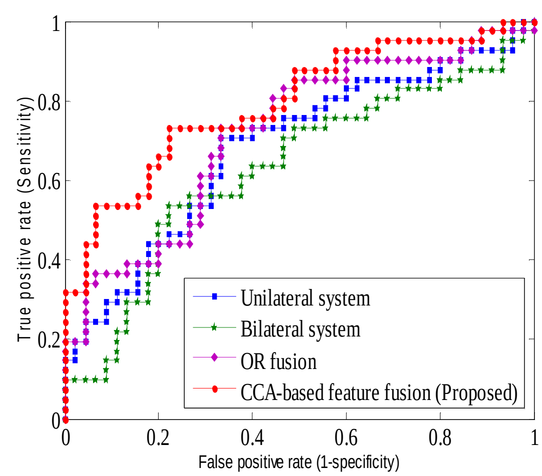

Figure 4 Comparison Of ROC Plots Of Various Systems

The merit of the proposed system in terms of false positive reduction which is the focus of this paper is illustrated in Table 2. Herein, the FPRs of various systems at true positive rates (TPR) of 60%, 65% and 70% are compared. It can be observed that the FPR for the proposed system is the least at these TPRs. The reduction in FPRs achieved by the proposed system at 65%, 70% and 75% TPRs is at least 39%, 35% and 33%, respectively when compared to the unilateral system, bilateral system and *OR* decision fusion.

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Table 2: Comparison Of Fprs At Tprs Of 60%, 65% And 70%

System	FPR (%)		
	TPR=60%	TPR=65%	TPR=70%
Unilateral	31	33	35
Bilateral	37	46	48
Best conventional fusion (*OR*)	28	31	33
CCA-based feature fusion (Proposed)	**17**	**20**	**22**

Though reduction of false positives is the primary focus of this paper, reduction of the misclassification of masses as normal regions is equally important so as to avoid delayed diagnosis and treatment. This can be measured as a reduction in the false negative rate (FNR) or equivalently increase in TPR. In Table 3, the TPRs of various systems are compared for different FPRs, i.e., 10%, 15% and 20%.

Table 3: Comparison of TPRs at FPRs of 10%, 15% and 20%

System	TPR (%)		
	FPR=10%	FPR=15%	FPR=20%
Unilateral	31	39	43
Bilateral	21	29	36
Best conventional fusion (*OR*)	36	39	41
CCA-based feature fusion (Proposed)	**53**	**56**	**63**

It can be observed from Table 3 that the highest TPR is achieved by the proposed system at these FPRs. The increase in TPRs achieved by the proposed system at 10%, 15% and 20% FPRs is at least 47%, 43% and 53%, respectively when compared to the unilateral system, bilateral system and *OR* decision fusion.

3. CONCLUSION

A new scheme that combines unilateral and bilateral analysis for reduction of false positives in the automated detection of mammographic masses has been proposed. The proposal employs CCA to determine directions in which the two feature sets are maximally correlated. The CCA-transformed features benefit from feature fusion as they are maximally correlated. The proposed scheme yields highly discriminative features and demonstrates an improved classification performance when compared to unilateral, bilateral and conventional-fusion based systems. The proposed system yields an FPR of 17%, 20% and 22% at TPRs of 60%, 65% and 70%, respectively. The corresponding FPRs for the best conventional-fusion based system are much higher and equal to 28%, 31% and 33%, respectively. The proposed system for false positive reduction can serve as a second pair of eyes and assist radiologists by improving their capability in analyzing breast cancer.

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