Bilateral Breast Volume Asymmetry in Screening Mammograms as a Potential Marker of Breast Cancer: Preliminary Experience

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ABSTRACT

The biological concept of bilateral symmetry as a marker of developmental stability and good health is well established. Although most individuals deviate slightly from perfect symmetry, humans are essentially considered bilaterally symmetrical. Studies have shown that if an individual is exposed to genetic mutations or environmental stresses, the homeostatic mechanisms that maintain symmetry of paired structures (such as breasts) tend to break down. Consequently, increased fluctuating asymmetry of paired structures could be an indicator of poor health. This preliminary study tested if bilateral morphological breast asymmetry in screening mammograms correlates with the presence of breast cancer. Following the biological definition of breast asymmetry in terms of volume, we applied automated computer algorithms for screening mammograms that segment the breast region and then measure each segmented breast's volume. These parameters were measured separately for each breast in each mammographic view (CC and MLO). Then, the normalized absolute differences of these parameters were investigated as measurements of fluctuating asymmetry (FA). Based on 268 cancer cases and 82 normal cases from the DDSM database, we observed that cancer patients demonstrate statistically significantly higher fluctuating asymmetry in their screening mammograms than patients with normal screening studies. Using an artificial neural network to combine FA measurements from both views along with the patient's age and breast parenchymal density resulted in an ROC area of 0.80±0.03. These results suggest that bilateral breast volume asymmetry estimated in screening mammograms should be studied as a risk factor for breast cancer.

Keywords: quantitative image analysis, risk assessment, mammography

I. INTRODUCTION

THE present study investigates the fluctuations in breast asymmetry using volume estimated from screening mammograms as a potential indicator of breast cancer. Evolutionary studies have shown asymmetry of paired body structures as a strong indicator of developmental stability and good health [1]. In general, potential risk factor can be calculated from different aspects the goal is to support computer assisted detection system and to provide inferences for diagnosis. Breast asymmetry measures and left/right breast analysis can provide significant information about the presence of a cancer. On the clinical site physicians have used early signs to indicate abnormalities. Early skin retractions, slight change in breast contour, edema of the skin, and/or vascular asymmetry are considered significant indications. At the engineering site, researchers have used asymmetry and fractal measures for the detection and characterization of lesions. However, the registration techniques that are used by these methods often face limitations in adequately addressing the complexities of the mammographic image formations. Lau and Bischof [2] applied a transformation based on the outline of the breast to detect tumors based on asymmetries in breast architecture. Nishikawa et al. [3] analyzed asymmetry densities to detect masses by performing a non-linear subtraction operation between the right and the left breast. Keddy and Brebner 1980 measured the maximum orthogonal breast dimensions on the CC and MLO views where they calculated the breast volume [4]. Katariya et al. 1974 assumed a conic shape from the using the CC view [5]. The study by Kalbhen et al. 1999 has used both view and information recorded from breast compression using volumes of 32 breast specimens [6]. They determined the most accurate method of calculating the volume of the breast. Assuming a half elliptic cylinder shape for the compressed breast for the CC view, the result reported better-measured volume than those assumed on the MLO view. Fluctuating asymmetry (FA), is used as a measure of phenotype-based deformation and it can be useful predictor. Low FA can successfully predict lower morbidity and or a transition stage. This is a preliminary investigation of this concept with respect to breast cancer. We have observed that mammographic estimates of bilateral breast volume asymmetry correlate highly with the presence of breast cancer.

II. METHOD

We performed computerized analysis of screening mammograms to derive measures of bilateral breast asymmetry. These measures included the height, width, and volume and they were calculated separately for each breast and each mammographic view. Figure 1 illustrates the height and width measures for each breast and from each mammographic view. The volume was estimated using formulas suggested in the literature. Although these formulas did not take into account the compression factor, studies have shown that the formulas we utilized correlate highly with true breast measurements made on mastectomy specimens. Specifically, in the CC view the breast volume was calculated assuming a conical shape for the breast. The suggested measurement originally proposed by [5]. The height h indicated on the CC view figure (a) present the maximum depth perpendicular to the chest wall at the proximal edge of the film. The breast width w represents the maximum breast outline at the proximal edge of the film. Accordingly the breast volume for the CC views is calculated as Volume $V = \pi \times \omega^2 \times h/12$. In the MLO views, the volume is calculated based on reference [6] using the formula $V=(h) \times (z)$. The breast height h is measured as the maximum breast depth distance from the nipple edge at the breast outline to the pictorial muscle. H is measured so that both measures w and z are perpendicular to h. the width w is the distance of the widest two points on the breast outline measured from the edge of the pictorial muscle. The intermediate width z is taken at the mid section. The algorithm start by allocating three points from the largest lower half of the breast.

Fluctuation in volumes for these views are calculated and normalized. Basically, we calculated bilateral breast differences, for the volume by taking the absolute difference between the left (L) and right (R) and correcting them according to breast size. These differences were utilized as measurements of fluctuating asymmetry

(FA): ${}_{relative}FA = |f_L - f_R| / (2 \times |f_L + f_R|)$.

Statistical analysis was performed to determine if the FA measures correlate with the presence of breast cancer. In addition, an artificial neural network (ANN) was explored as possible decision model to predict the presence of breast cancer using the FA measurements as well as the patient age and the breast parenchymal density. The ANN was trained and tested using 5-fold cross-validation using three nodes and six nodes ANN. Receiver Operating Characteristics analysis was used to evaluate the performance of the network and examine the significance of the estimated FA between the CC view and the MLO view.

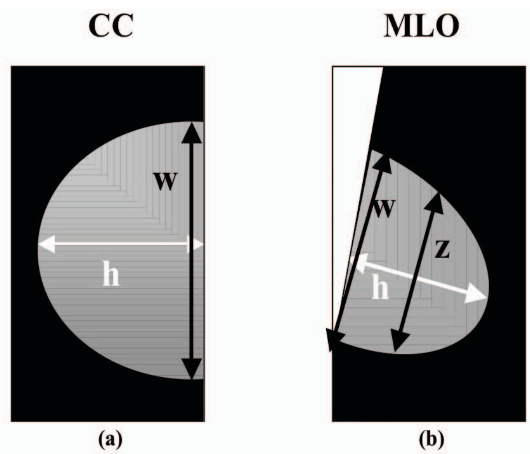

Fig. 1: (a) Breast measures for the CC vi ew (b) MLO breast measures

III. DATABASE

This analysis was performed on a database of 350 screening mammograms from the Digital Database of Screening Mammography (82 normal cases and 268 cases depicting malignant masses). For these cases both the cranio-caudal (CC) views and the mediolateral (MLO) views were analyzed. The images used were collected from the digital database of screening mammography (DDSM) a public database from Florida University.

IV. RESULT

The average fluctuating volume asymmetry was noticeably larger in cancer patients than in normal patients. But the difference was statistically significant only for the CC estimated FA.

CC view: FA(cancer) = 0.085±0.074 vs. FA(normal) = 0.056±0.044 (p-value<0.0001)

MLO view: FA(cancer) = 0.046±0.042 vs. FA(normal) = 0.038±0.032 (p-value=0.0688)

The following table shows the ROC and partial ROC areas achieved by the ANN. Using FA information from both views resulted in the best ROC performance.

TABLE 1: FA ROC area analysis and partial Az area index

ANN	Az	0.90Az
CC only	0.77 ± 0.03	0.24 ± 0.05
MLO only	0.73 ± 0.03	0.25 ± 0.05
Both views	0.80 ± 0.03	0.30 ± 0.05

Evolutionary studies have shown asymmetry of paired body structures as a strong indicator of developmental stability and good health. We have observed that mammographic estimates of bilateral breast volume asymmetry correlate highly with the presence of breast cancer. Figure 2 presents the ROC curves for the ANNs that rely on information from the CC and the MLO views. Figure 3 shows the performance difference of the ANN using three nodes versus using six nodes to evaluate the estimated FA using the CC and MLO views combined.

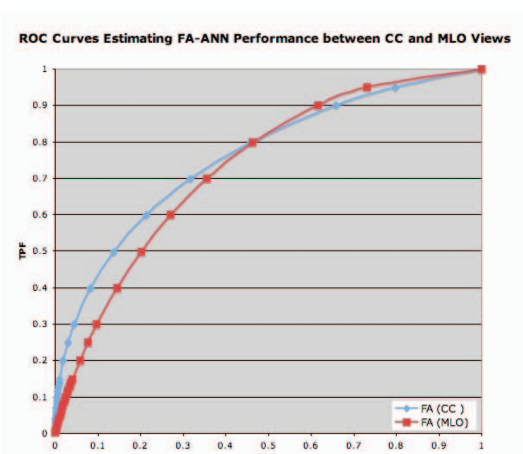

Fig. 2: ROC curves for the ANNs estimating FA for CC and MLO views

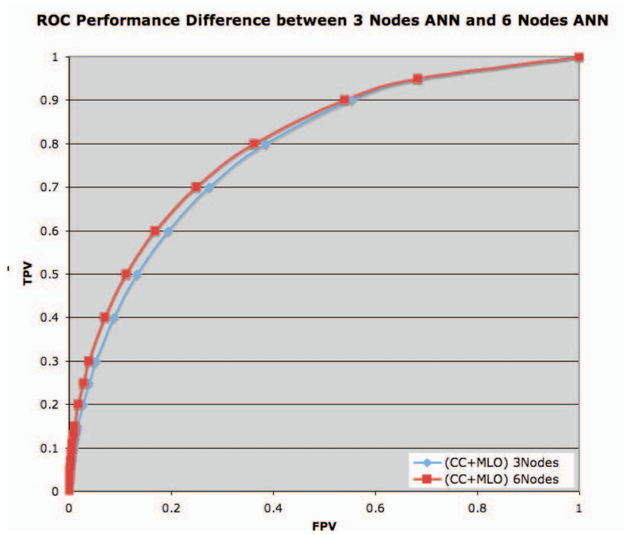

Fig. 3: ROC Performance Difference of the 3 Nodes vs the 6 Nodes ANN on the estimated FA for CC and MLO Combined

V. CONCLUSION

Recent clinical studies have shown that healthy cases with breast asymmetry are more likely to develop cancer. Asymmetry is normally a reflection of genetic transformation. This preliminary study suggests that the presence of breast cancer may be manifested in higher bilateral breast volume asymmetry that is measurable on a screening mammogram. More investigation on mammograms with benign masses as well as calcifications is in progress to further test the validity of the underlying hypothesis.

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