Computerized Medical Imaging and Graphics 38 (2014) 348–357

Contents lists available at ScienceDirect

Computerized Medical Imaging and Graphics

journal homepage: www.elsevier.com/locate/compmedimag

Prediction of near-term risk of developing breast cancer using computerized features from bilateral mammograms

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ARTICLE INFO

Article history:
Received 10 May 2013
Received in revised form
27 December 2013
Accepted 3 March 2014

Keywords:
Breast cancer
Mammogram
Computerized breast cancer risk analysis
Bilateral mammographic asymmetry feature
Near-term breast cancer risk assessment

ABSTRACT

Asymmetry of bilateral mammographic tissue density and patterns is a potentially strong indicator of having or developing breast abnormalities or early cancers. The purpose of this study is to design and test the global asymmetry features from bilateral mammograms to predict the near-term risk of women developing detectable high risk breast lesions or cancer in the next sequential screening mammography examination. The image dataset includes mammograms acquired from 90 women who underwent routine screening examinations, all interpreted as negative and not recalled by the radiologists during the original screening procedures. A computerized breast cancer risk analysis scheme using four image processing modules, including image preprocessing, suspicious region segmentation, image feature extraction, and classification was designed to detect and compute image feature asymmetry between the left and right breasts imaged on the mammograms. The highest computed area under curve (AUC) is 0.754 ± 0.024 when applying the new computerized aided diagnosis (CAD) scheme to our testing dataset. The positive predictive value and the negative predictive value were 0.58 and 0.80, respectively.

1. Introduction

Breast cancer is the most common cancer and second leading cause of cancer deaths of women [1]. Scientific evidence has shown that early cancer detection is important to enhance the survival rates of the patients through more effective patient management and treatment [2,3]. Since the majority of breast cancers are detected in women with no known risk factors defined in the existing epidemiology models [4,5], a uniform mammography screening program in the general population is currently applied and considered important [3]. However, due to the large variability in the depiction of breast abnormalities, the overlapping dense fibroglandular tissue on the projection images and the low cancer prevalence in the screening environment, both detection sensitivity and specificity of screening mammography are relatively low [6–8]. To help radiologists improve detection and diagnosis performances in reading and interpreting screening mammograms, a great amount of research has been conducted to develop CAD systems or schemes including our work on developing a variety of two-dimensional computerized image analysis algorithms optimized to enhance the performance of the traditional CAD systems during the last two decades (e.g., [9–13]). Currently, a number of commercialized CAD schemes, including the one originally developed in our group and then being licensed to Carestream Health, Inc. [14,15], are widely used in the clinical practice to assist radiologists in reading and interpreting mammograms to date.

However, a number of recently reported studies made the debate related to the efficacy (risk-benefit and cost-benefit) of population-based screening mammography more controversial [16,17]. Although reducing mammography screening interval (e.g., from annual screening to screening every two or more years) has the risk of missing early cancers, the currently frequent X-ray

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http://dx.doi.org/10.1016/j.compmedimag.2014.03.001
0895-6111/

mammography screening and the associated high false-positive recall rates contribute to higher cost as well as the unnecessary harms to many cancer-free women who routinely participate in the recommended mammography screening. As a result, since more scientists or researchers have realized the significance of establishing a more effective risk evaluation system to improve the accuracy of early breast cancer risk prediction, shifting the current population-based breast cancer screening paradigm to a new and optimal personalized screening paradigm in which women should be screened differently (including both the screening interval and screening imaging methods) has been attracting wide research interest [18,19,10,20,21]. To realize this ultimate goal, it is required to develop and establish breast cancer risk prediction or stratification models that have significantly higher (clinically acceptable) discriminatory power or positive predictive value (PPV) to stratify women into high and low risk groups of having or developing breast cancer in the near-term (e.g., ≤5 years). Hence, a small group of high risk women should be more aggressively screened and monitored for the early detection of breast cancer, while the majority of low risk women can be screened in a longer interval to reduce the potential harm (i.e., false-positive [22] and added cancer or other health risk [23]) until their risk statuses are changed. Unfortunately, all existing epidemiology based breast cancer risk models [5,24] do not have clinically acceptable accuracy for this purpose [25]. As a result, much innovative research work is needed to develop the new near-term risk models that are potentially clinically useful or acceptable for breast cancer screening purpose. Among the different efforts, previous studies have shown bilateral mammographic image feature asymmetry, the difference of imaged breast size [26] and average density between the left and right breast [27]. This might be a strong risk indicator of developing breast cancer in the near-term (e.g., the next sequential screening examinations) because such image phenotype variation may associate with genotype abnormality to break human natural bilateral symmetry in the paired morphological traits, including breasts, which may lead to cancer development. Instead of using registration or alignment techniques [27], designed global features from the whole breast area as the measurement of bilateral mammogram asymmetry. Thus the potential misalignment and poor registration between bilateral mammograms results from the differences in breast compression or positioning and changes in breast itself [28] are avoided. However, to the best of our knowledge, all the global asymmetry features are constraint in spatial feature domain, no global morphological features or textural features of asymmetry measurement are discussed in existing literatures.

In this study, the global morphological and textural asymmetry features are designed and we also investigate and test the possibility of converting and/or applying the traditional CAD schemes to breast cancer risk analysis schemes using the current negative mammograms (e.g., the negative mammograms acquired in the "prior" examinations) to predict the likelihood of women having high-risk breast lesions or cancers being detected in the near-term based on the computerized image feature analysis from the bilateral (left and right breast) mammograms. Our hypothesis is that the bilateral image feature difference computed from the left and right breasts should also provide useful information indicating the asymmetry of breast tissue structures that might be directly related to the development of high risk breast lesions.

2. Materials and methods

2.1. Database

From an established in-house full-field digital mammography (FFDM) image database, we randomly selected 90 pairs of bilateral mammograms, including 60 pairs of cranio-caudual (CC) view and 30 pairs of Mediolateral-oblique (MLO) view cases from 90 women who underwent routine screening mammography examinations. The women's ages range from 32 to 64, with a mean age of 43.7 years and median age of 43. Among the data, 4 cases, 28 cases, 49 cases and 9 cases were respectively rated by radiologists as almost entire fatty (BIRADS I), scattered fibro-glandular (BIRADS II), heterogeneously dense (BIRADS III) and extremely dense (BIRADS IV). All of these mammograms (treated as "prior" mammograms in this study) were interpreted as screening normal (without recall) by the radiologists; however, in the next sequential (annual) FFDM screening examinations, 34 of these women were recalled by radiologists due to the highly suspicious findings depicted on the FFDM images. Through additional imaging examinations and/or biopsies, 20 women were diagnosed and confirmed having cancer. The rest of the 56 women remaining screened negative (not recalled) during the sequential FFDM examinations (as shown in Table 1). In this study, 90 pairs of left and right FFDM images acquired from the "prior" negative examinations were used and analyzed. The goal of this study is to develop a new computerized scheme to classify risk assessment between 34 high risk women who developed abnormalities that were detectable by radiologists during the next sequential screening examinations and 56 low-risk women who remained cancer-free and were not recalled by radiologists in the next sequential screening.

Table 1
Distribution of our testing dataset.

Amount	Case		
	Results in first mammography exam	Results in second mammography exam	
	Normal	Stay normal	Turn abnormal
CC	60	39	21
MLO	30	17	13
Total	90	56	34

2.2. Breast cancer risk analysis scheme

The proposed breast cancer risk analysis scheme was developed to detect the cases with high possibilities of having highly suspicious breast abnormalities detected in the next sequential screening examinations. Specifically, the scheme was divided into four primary image processing and data analysis modules, including (1) image preprocessing, (2) region segmentation, (3) feature extraction and selection and (4) machine learning classification. Fig. 1 shows the flowchart of the proposed scheme.

2.2.1. Preprocessing module

In order to enhance image features and reduce image noise, we implemented the following three image preprocessing functions that could have impact on the following procedures as well as the final analysis results. These are (1) concurrent image enhancement; (2) concurrent multiorientation transform; and (3) concurrent multiresolution transform.

First, the image enhancement eliminates noise and artifacts by using adaptive tree-structured nonlinear filtering (TSF). In order to maximize the effect of TSF, the standardization method was used to convert the mammogram to match our algorithm [29]. Then we applied a central weighted median filter (CWMF) method and eight different variable filter windows to match different edge signals related to the breast tissues [30]. Compared to the preprocessing module in the single-view system, using either the right side mammogram or the left side mammogram, we need to process each pair of bilateral images at the same time and make sure each pair of corresponding parameters is the same. The CMWF and variable filter