Components of Computeraided Diagnosis for Breast Ultrasound

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Abstract

Although breast cancer has very high incidence and death rate, the cause of breast cancer is still unknown and there does not exist effective way to prevent the occurrence of breast cancer. Because early detection is a key role in breast cancer diagnosis and treatment, many imaging modalities are continually being developed to screen and diagnose the breast cancer at early stage. Especially, ultrasound (US) is one of useful diagnostic tools to distinguish benign from malignant masses of the breast, however, the ultrasound image has some limitations, such as low resolution and low contrast, speckle noise, and blurry edges between various organs. Recent progress of computer-aided diagnosis (CAD) system demonstrated that the application of CAD system could increase the diagnostic confidence for a physician and provides one possible solution to improve the positive predictive value of breast biopsy. The purposes of the paper are to review (1) the advantages and disadvantages of the most widely used breast imaging modalities and (2) each of CAD steps including preprocessing, segmentation, feature extraction and selection, classification and, evaluation. The last objective is (3) to discuss false positive reduction, whole breast ultrasound, elastography, and multi-modality CAD to further improve the performance of CAD.

Keywords: Computer-aided Detection, Computer-aided Diagnosis, Breast Imaging Modalities, Ultrasound, Breast Cancer

1 Introduction

Breast cancer starts in the breast cells of both women and men [73]. It is the fifth most common cause of cancer death [8]. According to the National Cancer Institute, an estimated 207,090 new cases and 39,840 deaths from breast cancer (only women) are expected to occur in the United States, despite recent advances in treatment [76].

Although breast cancer has very high incidence and death rate, the cause of breast cancer is still unknown [4]. No effective way to prevent the occurrence of breast cancer exists. Therefore, early detection is the first crucial step towards treating breast cancer and plays a key role in breast cancer diagnosis and treatment [39]. For example, given such circumstances, the 5-year survival rate for patients with breast cancer decreases from approximately 96% for cancers treated at an early stage to 77% for mid-stage cancers to just 21% for late-stage cancers that have spread to distant organs [50].

For better survival odds and reduced use of treatments and therapies and, fewer side-effects, many imaging modalities are continually being developed to diagnose the breast cancer at early stage currently using modalities include mammography, breast ultrasound, magnetic resonance imaging (MRI) and so on [73]. Especially, ultrasound (US) is one of useful diagnostic tools to distinguish benign from malignant masses of the breast [70], however, breast US remains controversial for screening because interpretation of the US images is greatly influenced by the scanning techniques and the sonographic features of

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the suspected abnormality. Thus the breast US exam is widely recognized to be one of the more difficult imaging procedures to perform and interpret [29]. There is a considerable overlap benignancy and malignancy in ultrasonic images and interpretation is subjective [11]. In addition, the screening will generate a large volume of US images and radiologists might tire while interpreting them.

The screening accuracy might be improved if a computer-aided diagnosis (CAD) system could assist radiologists by indicating the location of mass candidate regions [42] and diagnosing the detected lesions. For instance, to minimize the effect of the operator-dependent nature inherent in US, many computerized approaches have been proposed to assist differentiation between benign and malignant breast lesions [16], [9]. Recent progress of CAD system demonstrated that the application of CAD system could increase the diagnostic confidence for a physician and provides one possible solution to improve the positive predictive value of breast biopsy [11].

In the following sections of this article, we first describe the advantages and disadvantages of the most widely used breast imaging modalities in Section II. Then, in Section III, we reviewed each of CAD steps including preprocessing, segmentation, feature extraction and selection, classification and, evaluation. Finally, we discussed false positive reduction, whole breast ultrasound, elastography, and multi-modality CAD.

2 MODALITIES IN BREAST IMAGING

Because different situations call for different imaging tests, lots modalities are used for breast cancer screening and diagnosis. To focus on the CAD components, we briefly describe the effectiveness and limitation of well-known modalities in breast imaging such as mammogram, MRI, US. Then, BI-RADS method, which objectively describes the features of the masses in the images, is introduced and biopsy method is followed.

Mammography is the test of choice for screening women with no signs or symptoms of breast cancer. [51]. Thus, mammography is widely used in breast cancer screening. Its effectiveness in detecting breast cancer in women aged over 40 years has been established [26], [58]. However, mammogram has some limitations such that it is less effective for younger women or women with dense breast tissues [28] because small masses might be obscure in dense breast tissues [92]. Especially, younger women tend to have denser breasts and Asian women tend to have denser ones [42]. In addition, low-dose radiation from annual mammography screening may increase breast cancer risk [81]. As a result, approximately 65% of cases referred to surgical biopsy are actually benign lesions [49], [48].

Contrast-enhanced magnetic resonance imaging (MRI) can locate some small breast lesions sometimes missed by mammography [2]. It can also help detect breast cancer in women with breast implants and in younger women who tend to have dense breast tissue [51]. While MRI has a very high sensitivity for detecting lesions, its specificity is variable and often quite low because of the difficulty in distinguishing between benign and malignant lesions [21]. Therefore, it may lead to unnecessary breast biopsies. Also, it is expensive, less available, less comfortable for the patient, and cannot be used among those with pacemakers, or other internal metallic devices that are not compatible with the MRI [2].

A breast US is an imaging technique that sends high-frequency sound waves through breast tissues and converts them into images on a viewing screen. The US examination places a sound-emitting probe on the breast to conduct the test [39]. US is effective in distinguishing and characterizing breast masses set in a dense-breast-tissue environment, as in the case of young women [52]. Currently, breast US is primarily used for the diagnosis of breast cancer, as opposed to the screening of breast cancer. However, there is a growing need for US examination to be available for breast cancer screening in women with dense breast tissues [28]. One specific goal of diagnostic breast US is to minimize the number of biopsies that prove benign while maximizing identification of lesions that prove malignant on biopsy [74]. US is

more sensitive for detecting invasive cancer in dense Breasts. Most of all, there is no risk of cancer from radiation which is the most concerns in mammogram.

However, the US image itself has some limitations, such as low resolution and low contrast, speckle noise, and blurry edges between various organs, so it is more difficult for a radiologist to read and interpret an US image [39]. The obtained images are also poorly reproducible and screening examination takes a long time to scan an entire breast [42]. The main problems for the reader are fatigue and brief attention lapses. In some cases, viewing 5000 images at 10 frames per second requires 10 minutes. Maintaining concentration and focus for that long is exceedingly difficult [75].

The Breast Imaging Reporting and Data System (*BIRADS*) is a quality assurance tool originally designed to evaluate breast abnormalities for use with mammography later adapted for the MRI and Ultrasound by The American College of Radiology [1]. The system was designed to standardize patient reporting assessment categories, with a numerical code between 0 and 6, allowing for concise and unambiguous sharing of patient records between clinicians [84]. Because the risk of malignancy within the BI-RADS 4 category is so large (3%-94%), version 1 of the BI-RADS US Lexicon allows for voluntary subdivision of the BI-RADS 4 category into 4a, 4b, and 4c categories and in practice, the most challenging determination is between subgroup BI-RADS 3 and the BI-RADS 4a subgroup [74]. BI-RADS assessments for US (Table 1) are based on an analysis of descriptors from several feature descriptors (Table 2), with the most suspipcious feature dictating the US assessment and recommendation [67]. But it has proven difficult to teach the method, the quality of breast ultrasound is still regarded as highly operator dependent and many published reports show radiologists are uncomfortable with the number of benign and malignant masses that overlap in appearance [29].

BI-RADS US Category		Assessment and Management
0		Incomplete: additional imaging evaluation needed
1		Negative
2		Benign
3		Probably benign: short-interval follow-up recommended
4		Suspicious: biopsy
	4a	Low suspicion
	4b	Intermediate suspicion
	4c	Moderate suspicion
5		Highly suggestive of malignancy: biopsy
6		Known malignancy: treatment ongoing

Table 1: BI-RADS US Assessment Categories [67].

Although there are many diagnostic modalities, biopsy is the best way to do the differential diagnosis. For the lawful and safe reasons, surgeons perform an even increasing number of breast biopsies [11]. However, it is invasive and expensive. In addition, probability of positive findings at biopsy for cancer is low, between 10% and 31% [66], [54], [36].

3 Ultrasound Breast CAD

It is not always easy for a human observer to provide objective evidence of the benignity or malignancy of the tumor [3]. Although performance can often be improved by having two sonologists review US images, this strategy is not easily available [75]. On the other hand, computer vision techniques may help detecting some of them and supplying numerical measurements of the presence and relevance of abnormal factors [72], [57], [14].

Descriptor	Features Favoring Benign	Features Favoring Malignant	Indeterminate Features
Shape	Oval	Irregular, round	
Orientation	Parallel to skin	Not parallel to skin	
Margin	Circumscribed	Microlobulated, indistinct, angular, spiculated	
Lesion boundary	Abrupt interface	Echogenic halo	
Echo pattern	Anechoic, hyperechoic	Complex	Isoechoic, hypoechoic
Posterior acoustic features		Shadowing, combined pattern	Enhancement, no posterior acoustic features

Table 2: BI-RADS US Descriptors [67].

CAD has been developing fast in the last two decades. The main idea of CAD is to assist radiologists in interpreting medical images by using dedicated computer systems to provide second opinions. However, the final medical decision is made by the radiologists [28]. CAD is also defined as "the use of computer algorithms to aid the image interpretation process" [35]. CADe (Computer-aided detection) and CADx (computer-aided diagnosis) both have the same acronym, CAD. CADe is used for systems designed to aid the radiologist in the detection of visible findings that are suspicious for lesions. CADx refers to those systems that are designed to aid the doctors in the classification (or differential diagnosis) of detected lesions [5].

Studies on CAD systems and technology show that CAD can help to improve diagnostic accuracy of radiologists, lighten the burden of increasing workload, reduce cancer missed due to fatigue, overlooked or data overloaded and improve inter- and intra-reader variability [28]. Therefore, CAD is becoming an increasing important area for intelligent computer systems [37].

The role of CAD in US is to provide the second opinion for the interpretation of a sonographically detected breast tumor and to improve diagnostic confidence [50]. Interactive CAD could achieve high sensitivity and could more accurately determine if a lesion needed to be biopsied [80]. Therefore, varieties of CAD efforts have been attempted in the imaging evaluation of breast diseases [14].

CAD systems are mostly consist of several steps including preprocessing, segmentation, feature extraction and selection, classification, and evaluation. For each component, various computer algorithms have been developed and applied. In the next sub sections, the components of CAD system are described and the algorithms for each component are introduced.

3.1 Preprocessing

Because of an ultrasound's attenuation characteristics, identical textures at different depths have a different brightness, and the images are further corrupted by speckle noise.

Therefore, the first step in analyzing breast ultrasound image is preprocessing that suppresses the speckle noise [39]. On the other hand, edge-enhanced method is needed not to lose the important information for object boundaries and detailed structures in ultrasonic images [12], [32]. Finally, CAD should locate all suspicious nodules, before segmenting and analyzing the nodules.

An approach using 2D homogeneity and directional average filters to remove speckle noise was proposed [39]. However, speckle noise reduction-dedicated approaches usually use a low-pass filter to

reduce the speckle noise at the cost of blurring the edges [19]. Hence, other algorithms were needed to enhance and preserve the edge information for further image processing and analysis [11].

The edge detection problem can be modeled as a line process because boundaries between tissue layers appear as all sorts of lines in the ultrasonic images. Stick, as a set of short line segments of variable orientation, was therefore proposed to locally approximate the boundaries and to reduce speckles as well as improve the edge information in the ultrasound images [20]. The anisotropic diffusion filter [63] was used to get rid of the major drawback of the conventional spatial filters and improve the image quality significantly while preserve the important boundary information and then the stick method was applied to further reduce noise and enhance the edge information [11]. Also a fuzzy logic-based algorithm was presented to enhance the fine details of ultrasound image features, while avoiding noise amplification and over enhancement [39].

Multi-fractal analysis, single thresholding and a rule-based approach was used for the identification of the lesion ROI [89]. Also, the Probabilistic Boosting Tree (PBT), which involves the recursive construction of a tree, was used to train Adaboost classifier for detecting of a target object [90]. While a normal image consists of mainly near-horizontal edges, an abnormal image includes not only near-horizontal edges but also near-vertical edges around the border of a mass. Therefore, these near-vertical edges were detected by Canny edge detector as a cue to identify mass candidates and a location with two pair edges was determined as a mass candidates [43].

3.2 Segmentation

In order to identify the regions which will be processed in the further studies the interesting area and the background should be distinguished. In [3], segmentation of the nodule from the surrounding tissues was performed by means of a truncated median filter, a balloon algorithm and a dilation process. However, the conventional edge-based [7] and region-based methods [62] were unable to work well in segmenting ultrasonic images due to the existence of noise and speckle.

The level set approach [59] is a kind of deformable model. Comparing with other classical deformable model, such as snake [46], the principle of the level set approach is an active contour energy minimization that solves the computation of geodesics or minimal distance curves. It is governed by the curvature-dependent speeds of moving curves or fronts. There have been many successful ultrasound segmentation results using the level set approaches [18], [85], [17]. Another state-of-the-art active contour method, gradient vector flow (GVF) snake model, was also used to refine the initially mass boundary drawn by thresholding [89].

Other approaches were proposed in the literatures for nodule segmentation in US images. For example, the segmentation problem was transformed into clustering analysis by applying an automatic mass segmentation algorithm based on characteristics of breast tissue and eliminating particle swarm optimization (EPSO) clustering analysis [39]. In [43], mass candidates were segmented from the parenchymal background using the watershed algorithm. Also, a discriminative graph cut approach was proposed [90].

3.3 Feature Extraction and Selection

The general idea of CAD for breast US is to convert the visually extractable sonographic features into mathematic models and to characterize the lesions with the mathematic features based on the classification schemes [14]. Thus, it is one of the most important steps for CAD system to extract features from segmented masses.

Benign tumors usually have smooth shape and malignant tumors tend to have irregular border [11]. In detail, spiculation, taller than wide shape, angular margins, markedly hypoechoic appearance, acoustic

shadowing, calcifications, ramifications and microlobulations are considered as malignant findings which lead the physicians to carry out a biopsy. On the other hand, hyperechogenicity, ellipsoid shape, two or three gentle lobulations as well as a thin and echogenic capsule suggest the benignity of the nodule [3], [75].

Properly written CAD software should impose strict adherence to the BI-RADS Lexicon, decrease interobserver variability, and may even improve assignment of BI-RADS categories at least for less experienced breast sonologist [74]. Therefore, the BI-RADS sonographic characteristics including shape, orientation, margin, lesion boundary, echo pattern, and posterior acoustic feature classes are quantified into computerized features [71]. Morphological based US diagnosis of breast tumor take the advantage of nearly independent to either the setting of US system and different US machines [11]. Chen et al. proposed five new morphological features from segmented lesions including the number of substantial protuberances and depressions, lobulation index, elliptic-normalized circumference, elliptic-normalized skeleton, long axis to short axis ratio, and clinically useful indicators which are depth-to-width ratio and size of the lesion [14]. Other morphologic features were also extracted to account for such sonographic features including form factor, roundness, aspect ratio, convexity, solidity, and extent, respectively [11].

The regional features characterize the image properties evolved from the intensity distribution (eg, echogenicity, echotexture) [14], whereas the morphologic features describe the shape and contour of the lesion [11], [38]. The graylevels of the image represent the echo produced at each point when the ultrasound reaches it. These are the echogenicity of the nodule, the presence of acoustic shadow under the nodule, the microcalcifications and the observation of a thin echogenic capsule around the nodule [3]. Thus, texture features are helpful to classify benign and malignant tumors on sonography. The potential of sonographic texture analysis to improve breast tumor diagnosis has already been demonstrated [30]. The drawback of the texture analysis to classify tumors is usually performed well only in one specific ultrasound system due to its system-dependency [11]. Distance-based texture features instead of using conventional co-variance were proposed while residing in its calculation cost, which depends only on the size of the image treated and not on the number of gray levels. Moreover, it enables the extraction of visually perceptible physical parameters from the image [50].

Unlike the human vision system that uses the high-level image scene understanding to detect and classify suspicious lesions, the CAD scheme uses the extracted low-level pixel-based image features and the training dataset to build a machine learning classifier to detect and classify lesions. Therefore, the objective of feature selection is three-fold: improving the performance of the classifiers, building faster and more cost-effective classifiers, and providing better understanding of the underlying process of the generated data and classification [40].

These selected features are referred to as the substantial features. The classifier is then trained with the substantial features to determine the mathematic model that describes the relation of these features [14]. Although exhaustive search is a simple method that guarantees defining the optimal feature combination for the specific training and testing datasets, it requires heavy computational cost of search and comparison by times for n features. Hence, this method is unable to be used for practical applications. Consequently, many studies have been conducted in CAD development to search for the optimal feature set [60]. The substantial features were selected for each training data set on the basis of the forward sequential search approach [41] with the logistic discrimination function [22]. Also, the genetic algorithm (GA) may be used to be an effective tool for this purpose.

3.4 Classification

Artificial neural network (ANN) is a popular machine learning tool used in CAD schemes applying to the different medical images because of its advantages in learning the function to optimally approximate the relationship between the input features and desired classes using the relatively noisy or partially

available training data [61]. ANN is a general multilayer perceptron (MLP) neural network and the back propagation learning rule was used [27]. To identify whether a breast nodule is benign or malignant on ultrasound images, an ANN classification system was used [93], [15], [14], [44]. Once the essential features are selected by means of the discrimination function for a set of training data, the training data are used to train the ANN to divide the training data into benign and malignant categories [14]. Also, Bayesian neural network-based (BNN) classifier was applied to breast nodule classification [24], [38].

Decision tree models are commonly used in data mining to examine the data and to induce the tree and its rules, which will be used to help make predictions. The decision tree contains the decision node, branches, and leaves. Each branch leads either to another decision node or to the bottom of the tree, called a leaf node. Decision trees used to predict categoric variables are called classification trees. The decision tree model was used as a technique for mining the information for the diagnosis of breast cancer [50].

Support vector machines (SVM) [83], [13], [65] have been proposed as a very effective method for pattern recognition, machine learning and data mining. It is considered a good candidate because of its high generalization performance. Intuitively, given a set of points which belongs to either one of two classes, a SVM can find a hyperplane leaving the largest possible fraction of points of the same class on the same side, while maximizing the distance of either class from the hyperplane. According to [83], this hyperplane, called optimal separating hyperplane (OSH), can minimize the risk of misclassifying examples of the test set. For breast nodule classification nonlinear SVM with Gaussian radial basis kernel was applied [11].

3.5 Evaluation

One of the most generally used objective indexes to estimate the performance of diagnosis results is the accuracy $(TP+TN)/(TP+TN+FP+FN)$ along with the associated sensitivity $(TP/[TP+FN])$, specificity $(TN/[TN+FP])$, where TP, TN, FP, and FN is the number of true-positive findings, true-negative, false-positive, and false-negative, respectively [50], [14], [71]. For another performance comparison index, the Az (Area under ROC) values were used widely in evaluation of CAD systems because the best classification accuracy is not necessarily the preferred criterion for classification. Sometimes, one would rather have a higher sensitivity or specificity than have the best accuracy [14].

When the available sample size is limited in a pattern classification problem, one of the important questions is to determine what proportion of samples should be used for training the parameters of the classification system and what proportion should be used for testing. In general, the classification performance mainly depends on the training sample size, while the variance is mainly determined by the test sample size [87]. Different resampling methods, such as leave-one-out [24], [77], [38], k-fold cross-validation and bootstrapping, have been proposed [87].

4 Discussions

Breast cancer is one of the leading causes of death for women in many countries [64]. Current breast imaging modalities play a vital role in assisting clinicians in the primary screening of cancer, in the diagnosis and characterization of lesions, staging and restaging, treatment selection and treatment progress monitoring and in determining cancer recurrence [73]. Especially, US is cheap and safe from the radiation risk while mammography is less effective for younger women or women with dense breast tissues [28], and MRI is expensive and not widely available. However, US is heavily dependent on operator's experience. Also, reading an ultrasound image is tedious, hard work, which can lead to fatigue probably leading to an increased rate of misdiagnosis and missed diagnosis [39].

To be used in clinical practice, CAD should meet several demands such that it should save time, be seamlessly integrated into the workflow, not impose liability concerns, and especially improve radiologists' performance [82]. However, current CAD schemes still generate high false-positive detection rates that preclude their use as stand-alone diagnostic tools [25], [74] and also reduce their effectiveness as a "second reader" to assist radiologists. To reduce false positive rate, symmetry analysis can be used. Normal left and right breasts on same subject are architectural symmetry. The symmetrical feature is employed by radiologists as a useful tool in interpreting mammograms. Even if there is such a region like a mass, the region is classified normal tissue if same position in the other breast image has similar feature region [43]. Thus, the bilateral features can be utilized to differentiate the similarity and dissimilarity between tissues at corresponding locations in the bilateral views, and can be useful for improving the performance of a unilateral CAD system by further reducing the false positives [88].

Another practical method to reduce false positive rates is the limitation of the number of the cued-lesions. Since the performance of CAD schemes (in particular the number of false-positives) largely depends on the case difficulty [56], limiting the maximum number of suspicious lesions allowed to be cued for one examination is a commonly accepted practice. (Commercial CAD schemes also do this.) Studies have shown that this method improves overall performance of CAD schemes by substantially reducing the false-positive rate with a relatively small decrease in sensitivity [91], [45], [60].

Conventional hand-held ultrasound is generally used in breast screening. However, it is operator dependent [42]. Therefore, the obtained images are poorly reproducible, screening examination takes a long time to scan an entire breast, and some areas of the breast may not be scanned [42]. In order to overcome these problems, several automated US scanners have been developed [42]. A key advantage of an automated US system is standardized, reproducible and bilateral whole-breast imaging. This advantage could reduce the probability of missed diagnosis [86]. In addition, the recent ACRIN (American College of Radiology Imaging Network) indicate that whole breast ultrasound used in addition to screening mammography increases the sensitivity for cancer over mammography alone in women who are at high risk of breast cancer and who has dense breast tissue on mammography [47]. Apart from that, in the volumetric US images lesions may be overlooked. Therefore, there is a need to develop techniques to assist radiologists with the reading of volumetric breast US images, to allow for more efficient reading while avoiding that lesions are overlooked [78].

Palpation of the body is the classical method used by physicians to detect the presence of abnormalities that might indicate pathological lesions, usually because the mechanical properties of diseased tissue are typically different from those of the normal tissue that surrounds them [37]. Ultrasound elastography is a newly developed technique of imaging the tissue elasticity and it has been used clinically to examine a variety of breast lesions in patients [31], [53]. The principle of elastography is that the tissue compression produces the strain displacement within smaller strain in harder tissue and the larger strain in softer tissue [10]. The classification of elasticity images is, however, dependent on the examiner and significant inter-observer variability has been found in reader studies [79], [6], [68]. Therefore, a quantitative method or computer-aided analysis of elasticity images is needed to evaluate lesion stiffness objectively and to aid in the task of classification of benign and malignant breast tumors [55].

Although some features encountered in breast imaging can be seen across modalities, others are particular to the imaging modality [33]. Thus, to make a biopsy recommendation for a breast mass, radiologists routinely examine a patient's mammograms and the US images. These two modalities provide complementary information to the radiologists for more accurate diagnosis compared to that from a single modality [69]. In the same manner, computerized classification of cancer significantly was improved when lesion features from both mammography and ultrasound modalities were combined [23]. Therefore, it is a promising direction for future research to effectively integrate information from multiple modalities, which are becoming available for breast cancer detection [34] and diagnosis, such as US, MRI, and mammogram and so on. Combining computer analyses from multiple views or modalities

requires additional computer intelligence to determine the correspondence of lesions across views and modalities and an efficient means of conveying multimodality information to the radiologist [33].

References

[1] Imaging Reporting and Data System, BI-RADS, Lexicon. American College of Radiology, 2004.

[2] Breast MRI with and without Computer-Aided Detection (CAD). `http://www.ghc.org/all-sites/clinical/criteria/pdf/mri_breast_ca.pdf`, February 2013.

[3] M. Alemán-Flores, P. Alemán-Flores, L. Álvarez León, J. M. Santana-Montesdeoca, R. Fuentes-Pavón, and A. Trujillo-Pino. Computer-aided measurement of solid breast tumor features on ultrasound images. In *Proc. of The 8th European Conference on Computer Vision (ECCV 2004), Prague, Czech Republic, LNCS*, volume 3117, pages 353–364. Springer-Verlag, May 2004.

[4] P. Bandi, M. Boone, L. Brinton, S. Buchert, E. Calle, V. Cokkinides, E. Connor, R. Cowens-Alvarado, R. Elk, T. Gansler, L. McGinnis, T. Murray, C. Richard, C. Runowicz, C. Russell, D. Saslow, M. Shah, R. Smith, S. Summers, M. Thun, and E. Ward. Breast cancer facts & figures 2007-2008. Technical report, American Cancer Society, 2007.

[5] R. L. Birdwell. The preponderance of evidence supports computer-aided detection for screening mammography. *Radiology*, 253(1):9–16, October 2009.

[6] E. S. Burnside, T. J. Hall, A. M. S. G. K. Hesley, G. A. Sisney, W. E. S. J. P. Fine, J. Jiang, and N. J. Hangiandreou. Differentiating benign from malignant solid breast masses with us strain imaging. *Radiology*, 245(2):401–410, November 2007.

[7] J. Canny. A computational approach to edge detection. *IEEE Ttransactions on Pattern Analysis and Machine Intelligence*, 8(6):679–698, November 1986.

[8] W. H. O. M. centre. Cancer. `http://www.who.int/mediacentre/factsheets/fs297/en/index.html`, January 2013.

[9] R. F. Chang, W. J. Kuo, D. R. Chen, Y. L. Huang, J. H. Lee, and Y. H. Chou. Computer-aided diagnosis for surgical office-based breast ultrasound. *Archive of Surgery*, 135(6):696–699, July 2000.

[10] R.-F. Chang, W.-C. Shen, M.-C. Yang, W. K. Moon, E. Takada, Y.-C. Ho, M. Nakajima, and M. Kobayashi. Computer-aided diagnosis of breast color elastography. `http://adsabs.harvard.edu/abs/2008SPIE.6915E..18C`, April 2008.

[11] R. F. Chang, W. J. Wu, W. K. Moon, and D. R. Chen. Automatic ultrasound segmentation and morphology based diagnosis of solid breast tumors. *Breast Cancer Research and Treatment*, 89(2):179–185, February 2005.

[12] R.-F. Chang, W.-J. Wu, W. K. Moon, and D.-R. Chen. Automatic ultrasound segmentation and morphology based diagnosis of solid breast tumors. *Breast Cancer Research and Treatment*, 89(2):179–185, January 2007.

[13] O. Chapelle, P. Haffner, and V. N. Vapnik. Support vector machines for histogram-based image classification. *IEEE Transactions on Neural Networks*, 10(5):1292–1300, September 1999.

[14] C.-M. Chen, Y.-H. Chou, K.-C. Han, G.-S. Hung, C.-M. Tiu, H.-J. Chiou, and S.-Y. Chiou. Breast lesions on sonograms: Computer-aided diagnosis with nearly setting-independent features and artificial neural networks. *Radiology*, 226(2):504–514, February 2003.

[15] D. R. Chen, R. F. Chang, and Y. L. Huan. Computer-aided diagnosis applied to us of solid breast nodules by using neural networks. *Radiology*, 213(2):407–412, November 1999.

[16] D. R. Chen, R. F. Chang, and Y. L. Huang. Breast cancer diagnosis using self-organizing map for sonography. *Ultrasound in Medicine and Biology*, 26(3):405–411, March 2000.

[17] Y. Chert, S. Thiruvenkadam, H. Tagare, F. Huang, D. Wilson, and G. E. On the incorporation of shape priors into geometric active contours. In *Proc. of the 1st IEEE Workshop on Variational and Level Set Methods in Computer Vision, Vancouver, Canada*, pages 145–152. IEEE, July 2001.

[18] C. Corsi, G. Saracino, A. Sarti, and C. Lamberti. Left ventricular volume estimation for real-time three-dimensional echocardiography. *IEEE Ttransactions on Medical Imaging*, 21(9):1202–1208, September 2002.

[19] R. N. Czerwinski, D. L. Jones, and W. D. O'Brien. Edge detection in ultrasound speckle noise. In *Proc. of 1994 International Conference on Image Processing (ICIP'94), Texas, USA*, volume 3, pages 304–308. IEEE, November 1994.

[20] R. N. Czerwinski, D. L. Jones, and W. D. O'Brien. Detection of lines and boundaries in speckle images-application to medical ultrasound. *IEEE Transaction on Medical Imaging*, 18(2):126–136, February 1999.

[21] E. E. Deurloo, J. L. Peterse, E. J. Rutgers, A. P. Besnard, S. H. Muller, and K. G. Gilhuijs. Additional breast lesions in patients eligible for breast-conserving therapy by mri: impact on preoperative management and potential benefit of computerised analysis. *European Journal of Cancer*, 41(10):1393–1401, July 2005.

[22] W. R. Dillon and M. Goldstein. *Multivariate Analysis: Methods and Applications*. Wiley, 1984.

[23] K. Drukker, K. Horsch, and M. L. Giger. Multimodality computerized diagnosis of breast lesions using mammography and sonography. *Academic Radiology*, 12(8):970–979, August 2005.

[24] K. Drukker, C. A. Sennett, and M. L. Giger. The effect of image quality on the appearance of lesions on breast ultrasound: implications for CADx. `http://spie.org/x648.html?product_id=707743`, March 2007.

[25] C. Engelke, S. Schmidt, A. Bakai, F. Auer, and K. Marten. Computer-assisted detection of pulmonary embolism: performance evaluation in consensus with experienced and inexperienced chest radiologists. *European Radiology*, 18(2):298–307, February 2008.

[26] G. M. Freedman, P. R. Anderson, L. J. Goldstein, A. L. Hanlon, M. E. Cianfrocca, M. M. Millenson, M. von Mehren, M. H. Torosian, M. C. Boraas, N. Nicolaou, A. S. Patchefsky, and K. Evers. Routine mammography is associated with earlier stage disease and greater eligibility for breast conservation in breast carcinoma patients age 40 years and older. *Cancer*, 98(5):918–925, September 2003.

[27] J. A. Freeman and D. M. Skapura. *Neural Networks: Algorithms, Applications, and Programming Techniques*. Addison-Wesley Pub, 1992.

[28] H. Fujita, Y. Uchiyama, T. Nakagawa, D. Fukuoka, Y. Hatanaka, T. Hara, G. N. Lee, Y. Hayashi, Y. Ikedo, X. Gao, and X. Zhou. Computer-aided diagnosis: the emerging of three cad systems induced by japanese health care needs. *Computer Methods and Programs in Biomedicine*, 92(3):238–248, June 2008.

[29] M. Galperin, M. Andre, C. Barker, L. Olson, M. O'Boyle, K. Richman, and L. Mantrawadi. Reproducibility of image analysis for breast ultrasound computer-aided diagnosis. In *Proc. of the 29th International Symposium on Acoustical Imaging (Acoustical Imaging'29), Kanagawa, Japan, LNCS*, volume 29, pages 397–402. Springer-Verlag, November 2010.

[30] B. S. Garra, E. I. Cespedes, J. Ophir, S. R. Spratt, R. A. Zuurbier, C. M. Magnant, and M. F. Pennanen. Elastography of breast lesions: initial clinical results. *Radiology*, 202(1):79–86, January 1997.

[31] B. S. Garra, E. I. Cespedes, J. Ophir, S. R. Spratt, R. A. Zuurbier, C. M. Magnant, and M. F. Pennanen. Elastography of breast lesions: initial clinical results. *Radiology*, 202(1):79–86, January 1997.

[32] G. Gerig, O. Kübler, R. Kikinis, and F. A. Jolesz. Nonlinear anisotropic filtering of mri data. *IEEE Transactions on Medical Imaging*, 11(2):221–232, June 1992.

[33] M. L. Giger. Computer-aided Diagnosis in Diagnostic Mammography and Multimodality Breast Imaging. `http://facweb.cs.depaul.edu/research/vc/VC_Workshop2005/GigerRSNA04Chap.pdf`, November-December 2004.

[34] M. L. Giger, H.-P. Chan, and J. Boone. Anniversary paper: History and status of cad and quantitative image analysis: the role of med phys and aapm. *Medical Physics*, 35(12):5799–5820, January 2009.

[35] M. L. Giger, N. Karssemeijer, and S. G. Armato. Computer-aided diagnosis in medical imaging. *IEEE Transactions on Medical Imaging*, 20(12):1205–1208, December 2001.

[36] J. J. Gisvold and J. K. Martin. Prebiopsy localization of nonpalpable breast lesions. *American Journal of Roentgenology*, 143(3):477–481, September 1984.

[37] F. Gorunescu. Data mining techniques in computer-aided diagnosis: Non-invasive cancer detection. *International Journal of Biological and Medical Sciences*, 1(2):105–108, September 2007.

[38] N. P. Gruszauskas, K. Drukker, M. L. Giger, C. A. Sennett, and L. L. Pesce. Performance of breast ultrasound computer-aided diagnosis: Dependence on image selection. *Academic Radiology*, 15(10):1234–1245, October 2008.

[39] Y. Guo. *Computer-Aided Detection of Breast Cancer Using Ultrasound Images*. PhD thesis, Utah State University, May 2010.

[40] I. Guyon and A. Elisseeff. An introduction to variable and feature selection. *The Journal of Machine Learning Research*, 3:1157–1182, March 2003.

[41] D.-C. He, L. Wang, and J. Guibert. Texture discrimination based on an optimal utilization of texture features. *Pattern Recognition*, 21(2):141–146, March 1988.

[42] Y. Ikedo, D. Fukuoka, E. Takada, T. Endo, and T. Morita. Development of a fully automatic scheme for detection of masses in whole breast ultrasound images. *Medical Physics*, 34(11):4378–4388, November 2007.

[43] Y. Ikedoa, D. Fukuokab, T. Haraa, H. Fujitaa, E. Takadac, T. Endod, and T. Morita. Computerized mass detection in whole breast ultrasound images: Reduction of false positives using bilateral subtraction technique. `http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.104.1507&rep=rep1&type=pdf`, March 2007.

[44] S. Joo, Y. S. Yang, W. K. Moon, and H. C. Kim. Computer-aided diagnosis of solid breast nodules: use of an artificial neural network based on multiple sonographic features. *IEEE Transactions on Medical Imaging*, 23(10):1292–1300, October 2004.

[45] N. Karssemeijer, J. D. Otten, H. Rijken, and R. Holland. Computer aided detection of masses in mammograms as decision support. *The British Journal of Radiology*, 79(2):123–126, December 2006.

[46] M. Kass, A. Witkin, and D. Terzopoulos. Snakes: Active contour models. *International Journal of Computer Vision*, 1(4):321–331, January 1988.

[47] K. M. Kelly, J. Dean, W. S. Comulada, and S.-J. Lee. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. *European Radiology*, 20(3):734–742, March 2010.

[48] A. M. KNUTZEN and J. J. GISVOLD. Likelihood of malignant disease for various categories of mammographically detected, nonpalpable breast lesions. *Mayo Clinic Proceedings*, 68(5):454–460, May 1993.

[49] D. B. Kopans. The positive predictive value of mammography. *American Journal of Roentgenology*, 158(3):521–526, March 1992.

[50] W. J. Kuo, R. F. Chang, W. K. Moon, C. C. Lee, and D.-R. Chen. Computer-aided diagnosis of breast tumors with different us systems. *Academic Radiology*, 9(7):793–799, July 2002.

[51] E. L and L. J. Role of mri in breast cancer management. *Cleveland Clinic Journal of Medicine*, 76(9):525–532, September 2009.

[52] I. Leconte, C. Feger, C. Galant, M. Berlière, B. V. Berg, W. D'Hoore, and B. Maldague. Mammography and subsequent whole-breast sonography of nonpalpable breast cancers: The importance of radiologic breast density. *American Journal of Roentgenology*, 180(6):1675–1679, June 2003.

[53] H. T. Liu, L. Z. Sun, G. Wang, and M. W. Vannier. Analytic modeling of breast elastography. *Medical Physics*, 30(9):2340–2349, September 2003.

[54] R. M., H. K., J. N., H. W., R. R., R. E., and F. M. Use of fine needle aspiration for solid breast lesions is accurate and cost-effective. *The American Journal of Surgery*, 174(6):694–696, December 1997.

[55] W. K. Moon, J. W. Choi, N. Cho, S. H. Park, J. M. Chang, M. Jang, and K. G. Kim. Computer-aided analysis of ultrasound elasticity images for classification of benign and malignant breast masses. *American Journal of Roentgenology*, 195(6):1460–1465, December 2010.

[56] R. M. Nishikawa, M. L. Giger, K. Doi, C. E. Metz, F. F. Yin, C. J. Vyborny, and R. A. Schmidt. Effect of case selection on the performance of computer-aided detection schemes. *Journal of Medical Physics*, 21(2):265–269, February 1994.

[57] M. S. Nixon and A. S. Aguado. *Feature Extraction and Image Processing*. Academic Press, 2002.

[58] S. A. Norman, A. R. Localio, L. Zhou, A. L. Weber, R. J. Coates, K. E. Malone, L. Bernstein, P. A. Marchbanks, J. M. Liff, N. C. Lee, and M. R. Nadel. Benefit of screening mammography in reducing the rate of latestage breast cancer diagnoses united states. *Cancer Causes & Control*, 17(7):921–929, September 2006.

[59] S. Osher and J. A. Sethian. Fronts propagating with curvature-dependent speed: Algorithms based on hamilton-jacobi equations. *Journal of Computational Physics*, 79(1):12–49, November 1988.

[60] S. C. Park, B. E. Chapman, and B. Zheng. A multistage approach to improve performance of computer-aided detection of pulmonary embolisms depicted on ct images: Preliminary investigation. *IEEE Transactions on Biomedical Engineering*, 58(6):1519–1527, June 2011.

[61] S. C. Park, J. Tan, X. Wang, D. Lederman, J. K. Leader, S. H. Kim, and B. Zheng. Computer-aided detection of early interstitial lung diseases using low-dose ct images. *Physics in Medicine and Biology*, 56(4):1139–1153, February 2011.

[62] T. Pavlidis. *Algorithms for Graphics and Image Processing*. Computer Science Press, 1982.

[63] P. Perona and J. Malik. Scale-scape and edge-detection using anisotropic diffusion. *IEEE Ttransactions on Pattern Analysis and Machine Intelligence*, 12(7):629–639, July 1990.

[64] P. Pisani, D. M. Parkin, and J. Ferlay. Estimates of the worldwide mortality from 18 major cancers in 1985: implications for prevention and projections of future burden. *International Journal of Cancer*, 55(6):891–903, December 1993.

[65] M. Pontil and A. Verri. Support vector machines for 3d object recognition. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 20(6):637–646, June 1998.

[66] S. Raza, A. L. Goldkamp, S. A. Chikarmane, and R. L. Birdwell. The prevalence of carcinoma in palpable vs impalpable, mammographically detected lesions. *American Journal of Roentgenology*, 157(1):21–24, July 1991.

[67] S. Raza, A. L. Goldkamp, S. A. Chikarmane, and R. L. Birdwell. Us of breast masses categorized as bi-rads 3, 4, and 5: Pictorial review of factors influencing clinical management. *Radiographics*, 30(5):1199–1213, September 2010.

[68] D. M. Regner, G. K. Hesley, N. J. Hangiandreou, M. J. Morton, M. R. Nordland, D. D. Meixner, T. J. Hall, M. A. Farrell, J. N. Mandrekar, W. S. Harmsen, and J. W. Charboneau. Breast lesions: evaluation with us strain imaging–clinical experience of multiple observers. *Radiology*, 238(2):425–437, February 2006.

[69] B. Sahiner, H.-P. Chan, L. M. Hadjiiski, M. A. Roubidoux, C. Paramagul, M. A. Helvie, and C. Zhou. Multimodality CAD: combination of computerized classification techniques based on mammograms and 3D ultrasound volumes for improved accuracy in breast mass characterization. `http://spie.org/x648.html?product_id=535868`, May 2004.

[70] P. M. Shankar, J. M. Reid, H. Ortega, C. W. Piccoli, and B. B. Goldberg. Use of non-rayleigh statistics for the identification of tumors in ultrasonic b-scans of the breast. *IEEE TRANSACTIONS ON MEDICAL IMAGING*, 12(4):687–692, December 1993.

[71] W.-C. Shen, R.-F. Chang, W. K. Moon, Y.-H. Chou, and C.-S. Huang. Breast ultrasound computer-aided diagnosis using bi-rads features. *Academic Radiology*, 14(8):928–939, August 2007.

[72] M. Sonka, V. Hlavac, and R. Boyle. *Image Processing, Analysis, and Machine Vision*. PWS Publishing, 1999.

[73] S. V. Sree, E. Y.-K. Ng, R. U. Acharya, and O. Faust. Breast imaging: A survey. *World Journal of Clinical Oncology*, 2(4):171–178, April 2011.

[74] A. T. Stavros. New advances in breast ultrasound: Computer-aided detection. *Ultrasound Clinics*, 4(3):285–290, July 2009.

[75] A. T. Stavros, D. Thickman, C. L. Rapp, M. A. Dennis, S. H. Parker, and G. A. Sisney. Solid breast nodules: Use of sonography to distinguish between benign and malignant lesions. *Radiology*, 196(1):123–134, July 1995.

[76] Surveillance Epidemiology End Results Program. Seer cancer statistics review (csr) 1975-2010. Technical report, National Cancer Institute, 2013.

[77] T. Tan, B. Platel, H. Huisman, C. I. Sánchez, R. Mus, and N. Karssemeijer. Computer-aided lesion diagnosis in automated 3-d breast ultrasound using coronal spiculation. *IEEE Transactions on Medical Imaging*, 31(5):1034–1042, May 2012.

[78] T. Tan, B. Platel, R. Mus, L. Tabár, R. M. Mann, and N. Karssemeijer. Computer-aided detection of cancer in automated 3-d breast ultrasound. *IEEE Transactions on Medical Imaging*, 32(9):1698–1706, September 2013.

[79] A. Thomasa, S. Kümmela, F. Fritzscheb, M. Warmd, B. Eberte, B. Hammc, and T. Fischerc. Real-time sonoelastography performed in addition to b-mode ultrasound and mammography: Improved differentiation

of breast lesions? *Academic Radiology*, 13(12):1496–1504, December 2006.

[80] Łukasz Mendyk. Next Generation Service Delivery Platform. White Paper of COMARCH, January 2009. http://www.comarch.com/files_en/file_319/NextGenerationServiceDeliveryPlatform-IntegratedServiceFulfillment_Whitepaper_564.pdf.

[81] M. C. J. van der Weide, G. H. de Bock, M. J. Greuter, L. Jansen, J. C. Oosterwijk, R. Pijnappel, and M. Oudkerk. Mammography may increase breast cancer risk in some high-risk women. *Radiological Society of North America*, 213(2):413–422, November 1999.

[82] B. van Ginneken, C. M. Schaefer-Prokop, and M. Prokop. Computer-aided diagnosis: How to move from the laboratory to the clinic. *Radiology*, 261(3):719–732, December 2011.

[83] V. N. Vapnik. *The nature of statistical learning theory*. Springer-Verlag, 1995.

[84] C. L. Vaughan. New developments in medical imaging to detect breast cancer. *Continuing Medical Education*, 29(3):122–125, March 2011.

[85] X. Wang and W. G. Wee. A new deformable contour method. In *Proc. of the 10th International Conference on Image Analysis and Processing (ICIAP'99), Venice, Italy*, pages 430–435. IEEE, September 1999.

[86] Z. L. Wang, J. H. Xw, J. L. Li, Y. Huang, and J. Tang. Comparison of automated breast volume scanning to hand-held ultrasound and mammography. *Radiologia Medica*, 117(8):1287–1293, December 2012.

[87] J. Wei, H.-P. Chan, C. Zhou, Y.-T. Wu, B. Sahiner, L. M. Hadjiiski, M. A. Roubidoux, and M. A. Helvie. Computer-aided detection of breast masses: Four-view strategy for screening mammography. *The International Journal of Medical Physics Research and Practice*, 38(4):1867–1876, March 2011.

[88] Y.-T. Wu, L. M. Hadjiiski, J. Wei, C. Zhou, B. Sahiner, and H.-P. Chan. Computer-aided detection of breast masses on mammograms: bilateral analysis for false positive reduction. http://adsabs.harvard.edu/abs/2006SPIE.6144..683W, March 2006.

[89] M. H. Yap, E. A. Edirisinghe, and H. E. Bez. Fully automatic lesion boundary detection in ultrasound breast images. https://dspace.lboro.ac.uk/dspace-jspui/handle/2134/6499, March 2007.

[90] J. Zhang, S. K. Zhou, S. Brunke, C. Lowery, and D. Comaniciu. Database-guided breast tumor detection and segmentation in 2D ultrasound images. http://proceedings.spiedigitallibrary.org/proceeding.aspx?articleid=747899, February 2010.

[91] B. Zheng, J. K. Leader, G. Abrams, B. Shindel, V. Catullo, W. F. Good, and D. Gur. Computer-aided detection schemes: The effect of limiting the number of cued regions in each case. *American Journal of Roentgenology*, 182(3):579–583, March 2004.

[92] H. M. Zonderland, E. G. Coerkamp, J. Hermans, M. J. van de Vijver, and A. E. van Voorthuisen. Diagnosis of breast cancer: contribution of us as an adjunct to mammography. *Radiology*, 213(2):413–422, November 1999.

[93] J. M. Zurada. *Introduction to artificial neural systems*. West Group, 1992.

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