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Machine learning techniques for breast cancer computer aided diagnosis using different image modalities: A systematic review

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ABSTRACT

Background and objective: The high incidence of breast cancer in women has increased significantly in the recent years. Physician experience of diagnosing and detecting breast cancer can be assisted by using some computerized features extraction and classification algorithms. This paper presents the conduction and results of a systematic review (SR) that aims to investigate the state of the art regarding the computer aided diagnosis/detection (CAD) systems for breast cancer.
Methods: The SR was conducted using a comprehensive selection of scientific databases as reference sources, allowing access to diverse publications in the field. The scientific databases used are Springer Link (SL), Science Direct (SD), IEEE Xplore Digital Library, and PubMed. Inclusion and exclusion criteria were defined and applied to each retrieved work to select those of interest. From 320 studies retrieved, 154 studies were included. However, the scope of this research is limited to scientific and academic works and excludes commercial interests.
Results: This survey provides a general analysis of the current status of CAD systems according to the used image modalities and the machine learning based classifiers. Potential research studies have been discussed to create a more objective and efficient CAD systems.

1. Introduction

Breast cancer is one of the most common cancers diagnosed in women around the world and it is a main cause of fatality among women. In low-income and middle-income countries the mortality rates are relatively high compared to developed countries. According to the World Health Organization's International Agency for Research on Cancer (IARC) 2013 report, more than 1.7 million women in 2012 were diagnosed with breast cancer worldwide. This is considered around 11.9% of all cancers diagnosed in the same year with 522,000 death cases reported. It is also expected that by 2025 there will be 19.3 million new cancer cases [1,2]. Moreover, in developing countries like Egypt, the dense population and the patients' ignorance to the disease symptoms and seeking medical consultation either when it's too late or extremely critical leads to higher mortality. Also, shortage of medical specialists and experts in rural areas adds up to the problem of early and accurate diagnosis of breast cancer causing higher mortality rate. Using information technology and medical data to build medical support systems which can mimic the doctor's reasoning and conclude the symptoms is one solution to breast cancer early detection and hence increase the treatment chances and decrease mortality rate.

Medical image examination is the most effective method for diagnosis of breast cancer. Different medical imaging modalities are used for diagnosis such as: digital mammogram (DM), ultrasound (US), magnetic resonance imaging (MRI), microscopic (histological) images, and Infrared thermography (IRT). As a means to assist radiologists and physicians in identifying abnormalities, these modalities produce images which have reduced mortality rates by 30–70% [3]. Images interpretation is operator-dependent which requires expertise, thus using information technology is a necessity to accelerate and enhance the accuracy of the diagnosis providing a second opinion to the expertise [4]. Using some computerized features extraction and classification algorithms formulated as computer-aided diagnosis/detection (CAD) can be a great helpful tool for physicians and experts in detecting abnormalities.

Many efforts were made to develop CAD systems which are based on the advances of digital image processing, pattern recognition and artificial intelligence. The CAD systems are expected to overcome the operator dependency, increase diagnosis rate, and re-

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duce the expense of medical complementary modalities [5–7]. And thus it may help to reduce false positive reactions that may lead to futile treatment and psychological, physical, and economic costs that come with a false positive. And it also may reduce false negative readings that may cause omission of treatment that could result in remissions. It is reported that the detection sensitivity without CAD is around 80% and with it sensitivity reaches 90% [8]. In 2011, Sadaf et al. [9] studied the performance of full-field digital mammography (FFDM) augmented with CAD tools. The study showed that CAD combined with mammography presented 100% sensitivity in identifying cancers manifesting as microcalcifications and 86% sensitivity for other mammographic appearances of cancer. Accordingly, CAD has become the most active field of research in medical imaging to improve the precision of a diagnosis [10–12].

Computer aided detection is concerned with using a computer output to determine the location of suspect lesions. Afterwards, the radiologists are the one who is in charge of the characterization and diagnosis of the abnormalities as well as the patient management. Computer aided diagnosis on the other hand takes the detection done by a human or a computer and gives an output that determines the characterization of the lesion and gives the probability of malignancy and any abnormalities [13].

In general, a complete CAD system involved segmented structures, the detection of abnormalities and the extraction of their characteristics for a subsequent classification of the problem. Thus, the CAD systems can be categorized into four major stages. The first stage is preprocessing to prepare the images for the subsequent stages such as cleaning the medical image and removing noise from it through a set of image preprocessing operations. The second stage is the segmentation of the region of interest (ROI) in the image, which is a procedure of dividing the input image into several regions according to the visual characteristics. The third stage is the features extraction and selection where features are extracted from the cleaned images then the most discriminative features are selected. The selected features are capable of differentiating between normal and cancerous regions in order to minimize the classification error. Despite large effort, there is still no agreement on the features that are most suitable for this task. Many kind of features such as dynamic features, textural features, and morphological features have been traditionally used in tumor classification [14]. These selected features are organized in a database as an input to the classification stage. The final stage in the CAD system is the classification that is regarded as the heart of the CAD. It is a data mining process that assigns labels or classes to different groups, whose aim is to discover and extract hidden patterns from large datasets using different Machine Learning Technique (MLT) [15,16]. The generated model or patterns are used to predict the future unknown cases. Many MLTs have been used in the medical domain such as: K-nearest neighbors (K-NN) [17], Artificial Neural Network (ANN) [18,19], Decision Tree (DT) [20, 21], and Support Vector Machine (SVM) [22,23]. The selection of an appropriate MLT to build a classifier responsible for separating different kind of breast lesions is the key component of the development of CAD systems [14].

The contribution of this systematic review is to present the state of the art proposed in the literature that focuses on different machine learning techniques used for the classification of breast tumor lesions. Different statistical analysis of different aspects of the CAD systems presented in the selected papers are conducted using charts, rather than just presenting a short summary of all studies. The paper is organized as follows: the "Methodology" in Section 2 presents the process of conducting the review. The "Results" are presented in Section 3. The "Discussion" is presented in Section 4. And finally the paper is concluded in Section 5, and some points of future work are recommended.

2. Methodology

2.1. Search criteria

This systematic review aims to identify various studies related to breast cancer CAD systems based on medical images and MLT classifiers. The primary aim of this review is to find the answer of the following research questions:

- What are the MLT classifiers currently applied for breast cancer CAD systems based on medical imaging?
- What are the modalities of medical imaging used for the development of breast cancer CAD systems?
- What are the evaluation criteria used for the assessment of breast cancer CAD systems?
- What are the data sets used for the development of breast cancer CAD systems?

Several electronic databases were searched, Springer Link (http://www.springerlink.com), Science Direct (Elsevier) (http://www.sciencedirect.com), IEEE Xplore (http://www.ieeexplore.ieee.org, and (https://www.ncbi.nlm.nih.gov/pubmed/). The following search keywords were used: "breast cancer", "image", "learning", "classification", "classifier", "classify", "computer-aided diagnosis", "computer-aided detection", "computer-assisted diagnosis", and "CAD". Maximum possible number of publications was investigated through the years from 2012 to January 2017. However, some relevant studies may have been skipped unintentionally. The searching strategy is designed according to different databases searching standards. Table 1 presents the compositions of terms used according to the search engine of each database aiming to obtain all possible existing literature work.

All relevant studies were investigated, but only studies that satisfied the following inclusion criteria are included: (1) breast cancer is the only disease considered (other diseases are excluded); (2) at least one MLT is used as a classifier; (3) at least one of different medical imaging modalities is used (other diagnosis techniques are excluded); (4) the most common performance measures of the applied classifiers are reported (5) all paper articles must be a full complete paper (abstracts only are excluded); (6) work published in between 2012 to January 2017. Some other relevant studies are excluded such as surveys, books, letters, and non English articles. The search was carried out between December 2016 and January 2017. Initially, large amount of research articles was collected due the broadness of the subject under study "computer aided diagnosis/detection". Totally, 320 studies were retrieved. In the second step, articles irrelevant to the inclusion search criteria are removed. So, only 154 studies (48.125%) are included while the rest 166 studies are not fitted well with the predefined search criteria and these articles are excluded from the retrieved list. In this SR, the information extracted from each study included the used imaging modality, machine learning techniques which are used as classifier, scope of the included study, results using the performance criteria, data sets and number of images/cases used if available. Fig. 1 shows a flow diagram which summarizes the selection of the retrieved studies. It should be noted that many articles include more than one MLT, and they were all counted when constructing the corresponding diagrams.

During the search, a significant variety of medical publications, computational intelligence, image processing and pattern recognition were observed. All retrieved articles have been published in journals of Springer Link, Science Direct, and PubMed. According to IEEE search, most IEEE studies are conference proceedings and are included in this SR. Table 2 shows the details of journals name, publishers and number of articles being published in each journal. From this table, it is shown that: (1) 17 journals published in Springer Link are considered; (2) 15 journals are published in

Table 1
Composition of search terms.

Literature sources	Search in	Search terms
Springer Link	Search Command	("breast cancer") AND ("image") AND ("classification" OR "machine learning" OR "classifier" OR "learning") AND ("computer-aided diagnosis" OR "computer aided detection" OR "computer assisted diagnosis" OR "CAD")
Science Direct	Title, Abstract, Keywords	(("Breast cancer" AND "image") AND ("learning" OR "classification" OR "classifier" OR "classify")) AND ("computer aided diagnosis" OR "computer aided detection" OR "computer assisted diagnosis" OR "CAD")
IEEE	Title, Abstract, Keywords, "Metadata"	"Breast cancer" AND "image" AND ("learning" OR "classification" OR "classifier" OR "classify") AND ("computer aided diagnosis" OR "computer aided detection" OR "computer assisted diagnosis" OR "CAD")
PubMed	All Fields	("Breast cancer" AND "image") AND ("learning" OR "classification" OR "classifier" OR "classify") AND ("computer aided diagnosis" OR "computer aided detection" OR "computer assisted diagnosis" OR "CAD")

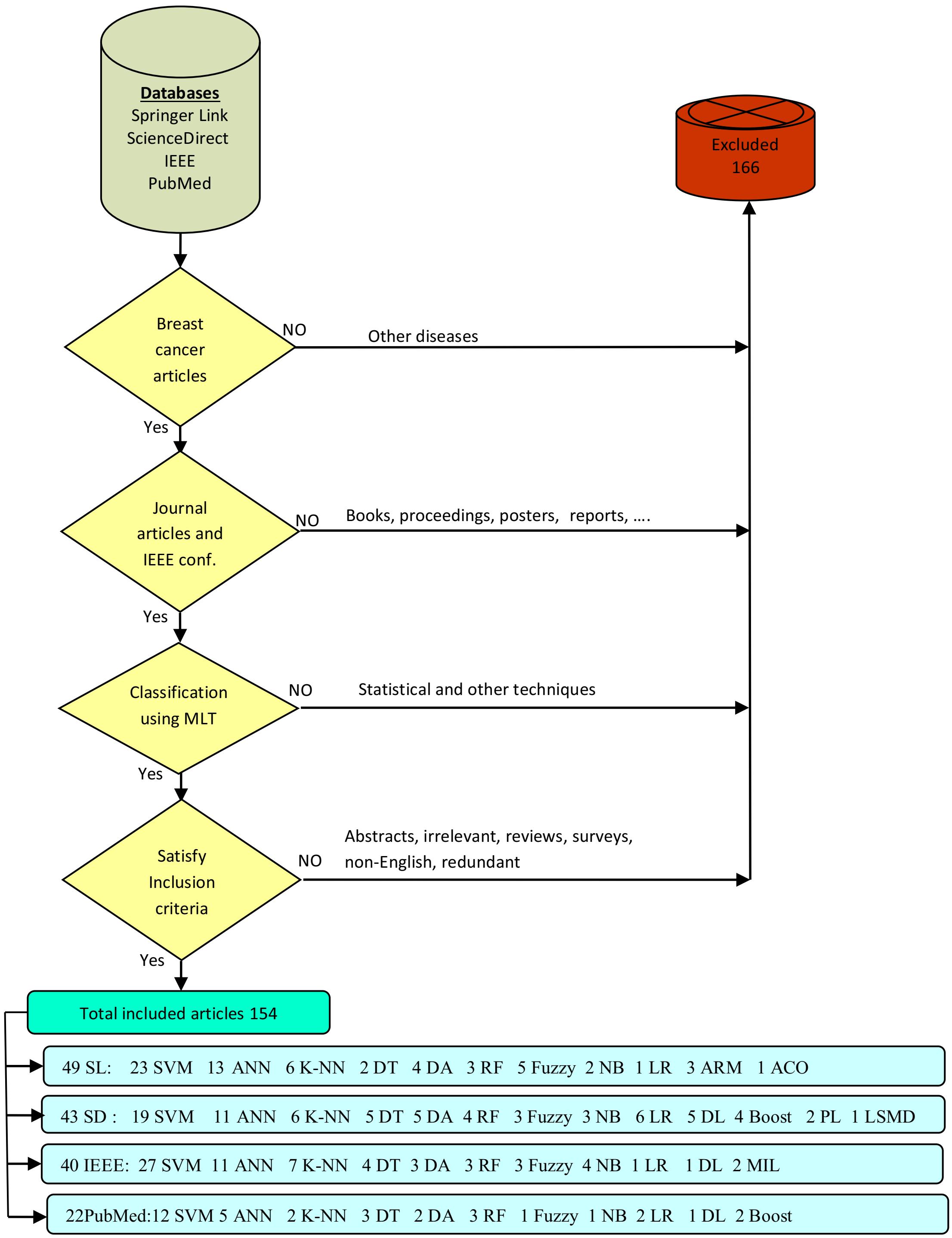

Fig. 1. Flow diagram summarizes the selection of the retrieved studies.

Table 2
List of used journals and the corresponding number of papers.

Springer journals	Science Direct journals	PubMed journals	IEEE journals
Journal of Digital Imaging (9)	Computer Methods and Programs in Biomedicine (9)	Medical Physics (6)	Transactions on Medical Imaging (1)
Journal of Medical Systems (8)	Computers in Biology and Medicine (7)	Computational and Mathematical Methods in Medicine (3)	Systems Journal (1)
Neural Computing and Applications (8)	Expert Systems with Applications (5)	Radiology (2)	Transactions on Fuzzy Systems (1)
International Journal of Computer Assisted Radiology and Surgery (4)	Ultrasound in Medicine and Biology (5)	Technology and Health Care (1)	Transactions on Systems, Man, and Cybernetics-Part A: Systems and Humans (1)
Multimedia Tools and Applications (3)	Neurocomputing (4)	Journal of Medical Imaging (1)	IEEE Transactions on Biomedical Engineering (1)
BioMedical Engineering OnLine (3)	Medical Image Analysis (2)	Studies in Health Technology and Informatics (1)	
EURASIP Journal on Advances in Signal Processing (3)	Ultrasonics (2)	Physics in Medicine and Biology (1)	
European Radiology (2)	Computerized Medical Imaging and Graphics (2)	Bio-Medical Materials and Engineering (1)	
Sādhanā (1)	Applied Soft Computing (1)	Journal of Medical Engineering and Technology (1)	
Journal of Medical Ultrasonics (1)	Information Sciences (1)	Journal of Magnetic Resonance Imaging (1)	
Biomedical Engineering Letters (1)	Engineering Applications of Artificial Intelligence (1)	Journal of Visualized Experiments (1)	
Evolving Systems (1)	Procedia Computer Science (1)	Journal of Engineering in Medicine (1)	
Human-Centric Computing and Information Sciences (1)	Artificial Intelligence in Medicine (1)	Computer Methods in Biomechanics and Biomedical Engineering (1)	
BMC Cancer (1)	Journal of Applied Logic (1)	Journal of Clinical Ultrasound (1)	
Memetic Computing (1)	Academic radiology (1)		
BMC Medical Imaging (1)			
EURASIP Journal on Image and Video Processing (1)			

Science Direct; (3) 14 journals are published in PubMed in addition to those found in Springer Link, Science Direct, IEEE and are found also in PubMed; (4) only five journals published by IEEE are included, each contains 1 paper. As shown in Table 3, there are many IEEE conference papers included. To be precise, a total of 35 papers are collected from IEEE conference proceedings. Regarding PubMed it was found that its search results contain (18) papers published by Springer Link, (31) papers published by Science Direct, and (6) papers published by IEEE, so these papers are excluded from PubMed as they have already been included in the other three databases. After excluding these papers, it was found that there are 14 journals included in PubMed. These journals have been added as PubMed journals as they are collected through PubMed search.

2.2. Data extraction

The data extracted from the selected articles are presented in Tables 4–7 which present the search results for Springer Link, Science Direct, IEEE, and PubMed respectively. In the investigated literature, it is found that the frequent problems in breast cancer are: (1) classification between normal and abnormal tissues, (2) classification of abnormal tissue to benign and malignant, (3) classification of breast tissue into dense and fatty tissue, and (4) positive and negative lymph node classification. To solve these problems, five number of image modalities are used: DM, US, MRI, microscopic (histological) images, and infrared thermography (IRT). A total of 16 MLTs are used in the presented literature which are: SVM, ANN, K-NN, Decision tree (DT), Discriminant Analysis (DA)(Quadratic DA (QDA), and Linear DA (LDA)), Random Forest (RF), Fuzzy classifier, Naïve Bayesian (NB), Logistic Regression (LR), Deep learning (DL), Ensemble learning, Association Rule Mining (ARM), Polynomial classifier (PL), Multiple Instance Learning (MIL), Ant Colony Optimization (ACO), and Least Square Minimum Distance (LSMD). For evaluation of CADs, the most common used performance measures in the literature are: Accuracy (Acc), Sensitivity (Sn), Specificity (Sp), and Area Under the Curve (AUC).

3. Results

This SR reviewed the publications of CAD systems from 2012 till January 2017. It was found that a commonly used framework in most of the publications under study includes 4 stages which are preprocessing, segmentation, features extraction and selection, and finally the classification stage that is regarded as the heart of the CAD. In this SR our interest was the usage of different MLTs as classifiers for CADs system of breast cancer.

This section presents the analysis of the results shown in Tables 4–7. In this section, the used modalities, MLTs, performance criteria, and datasets are shortly declared. The proposed work covered the period from 2012 to January 2017. Fig. 2 indicates the rate of publication in this time period. Although breast cancer CAD system is not a new topic, it is clear that the number of its publications is varying slowly over time and it can still be increased in the next time stage. From the bar chart it is shown that the trend is an increased interest in the CAD systems research. The year 2015 has the largest number of publications. Even though a decrease in number of publications is observed in 2016 compared to 2015, still the number of publications in 2016 is stable or a little bit more than the years 2012–2014. Also it is shown that only for the month January 2017 the number of publications is 6 papers, so it is expected to have an increase in number of publications in 2017. Also it is noted from Tables 4–7 that the new trend of deep learning started to be used in 2016 and 2017 which shows an increased interest recently in applying deep learning in CAD systems.

Table 3
List of IEEE conferences.

Name of used IEEE conferences
Society of Instrument and Control Engineers of Japan (SICE), 2016 55th Annual Conference of the
Information Science and Technology (CiSt), 2016 4th IEEE International Colloquium on
Advanced Robotics and Mechatronics (ICARM), International Conference on
Evolutionary Computation (CEC), 2016 IEEE Congress on
Programming and Systems (ISPS), 2015 12th International Symposium on
Intelligent Systems and Control (ISCO), 2015 IEEE 9th International Conference on
2015 IEEE Congress on Evolutionary Computation (CEC)
2015 IEEE 28th International Symposium on Computer-Based Medical Systems
2015 CHILEAN Conference on Electrical, Electronics Engineering, Information and Communication Technologies (CHILECON)
Computer, Communications, and Control Technology (I4CT), 2015 International Conference on
Image Processing (ICIP), 2015 IEEE International Conference on
2015 IEEE 12th International Symposium on Biomedical Imaging (ISBI)
Information and Communication Technology, Electronics and Microelectronics (MIPRO), 2015 38th International Convention on
Computing, Control, Networking, Electronics and Embedded Systems Engineering (ICCNEEE), 2015 International Conference on
2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (1)
2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (2)
2015 IEEE 12th International Symposium on Biomedical Imaging (ISBI)
2015 International Conference on Advances in Biomedical Engineering (ICABME)
2015 27th International Conference on Microelectronics (ICM)
Computational Intelligence in Healthcare and e-health (CICARE), 2014 IEEE Symposium on
2014 22nd Iranian Conference on Electrical Engineering (ICEE)
Intelligent Systems: Theories and Applications (SITA-14), 2014 9th International Conference on
IWSSIP 2014 Proceedings
2014 International Conference on Computer, Control, Informatics and Its Applications
Information Technology and Electrical Engineering (ICITEE), 2014 6th International Conference on
Control, Instrumentation, Communication and Computational Technologies (ICCICCT), 2014 International Conference on
Soft Computing and Pattern Recognition (SoCPaR), 2014 6th International Conference of
Multimedia Computing and Systems (ICMCS), 2014 International Conference on
2013 IEEE International Conference on Image Processing
Bioinformatics and Bioengineering (BIBE), 2013 IEEE 13th International Conference on
Visual Communications and Image Processing (VCIP), 2013
Systems, Signal Processing and their Applications (WoSSPA), 2013 8th International Workshop on
Image Analysis and Interpretation (SSIAI), 2012 IEEE Southwest Symposium on
Multimedia Computing and Systems (ICMCS), 2012 International Conference on

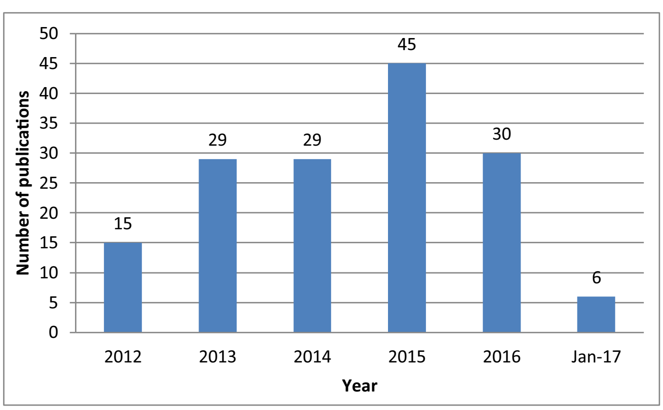

Fig. 2. Number of papers published on CADs from 2012 to January 2017 using specified criteria.

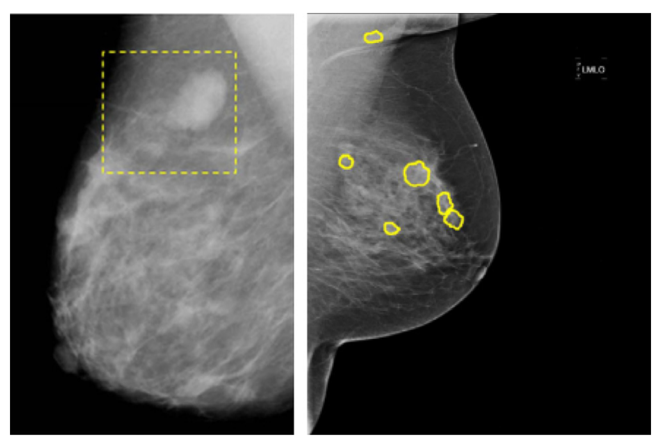

Fig. 3. Samples of DM images used in publications of the proposed SR (adapted with permission from Springer Publisher from Ref. [24] and with permission from Elsevier Publisher from Ref. [73]) [24,73].

3.1. Image modalities

Different image modalities are used to examine the presence of breast cancer nowadays. The image modalities investigated in this SR are:

DM is the most commonly and important used screening technique in clinical practice. It has the capability of detecting tumors before they develop further and become easily detected and felt by the physician. Although the DM has drawbacks as being an inappropriate screening technique for ladies with dense breasts because it uses ionizing radiations, still X-ray mammography is the standard breast cancer screening method that offers high 2D resolution. Thus DM is able to detect very small variations in composition of the tissues as micro-calcifications [177]. DM is used extensively in the proposed SR where out of 154 used papers there are 98 papers that depend on DM to classify breast cancer tissues. Fig. 3 shows samples of DM images used in different publications of the proposed SR.

US is a convenient modality for cancer detection for ladies having dense breasts. Moreover, it is useful for tumor detection when getting negative mammography. US evaluates the size of tumor and it can characterize abnormalities discovered by DM. On the other hand, its capability of discovering contra-lateral malignant lesions is limited [178]. Elastography and shear wave elastography are a developing form of US. Number of papers included in the presented SR that adopt US images for detecting and diagnosing of

Table 4
Springer Link search results.

Reference	Imaging modality	Machine learning technique	Scope	Evaluation results	Image data sets
[24]	DM	KNN	classifying ROI as normal or abnormal	Acc = 92.81% ± 0.0093, Sn = 92.85% ± 0.0099, AUC = 0.9713	IRMA MIAS
[25]	DM	SVM	classifying normal and masses classifying benign and malignant	average Acc from 68 to 100%	MIAS 109 cases
[26]	DM	Associative classifier with fuzzy-ANN	classification of breast tissues and masses	Acc = 95.11%, Sn = 92.22%,Sp = 96.39	DDSM 170 benign 130 malignant
[27]	DM	Fuzzy Gaussian Mixture Model (FGMM)	classify into malignant or benign	Acc = 93%, Sn = 90%, Sp = 96%	DDSM 300 images
[28]	DM	SVM RF NB	predicting benign/malignant lesions, dense/fatty tissue classification, finding identification (mass / microcalcification distinction)	benign/malignant: ACC = 89.3% to 64.7% dense/fatty tissue: ACC = 75.8% to 78.3% finding identification: ACC = 71.0% to 83.1%	INbreast BCDR
[29]	DM	SVM	classify abnormalities using fusion features	Acc = 93.17%, Sn = 92.71%, Sp = 93.46%	MIAS
[30]	US	KNN	diagnose non-mass lesions appearing as hypoechoic areas	Sn = 87.8%, Sp = 89.5%, AUC = 0.93	Private 97 cases
[31]	DM	Adaptive Differential Evolution Wavelet-ANN (Ada-DEWNN)	classification of benign/malignant breast tissues.	MIAS: Acc = 89.38%, Sn = 83.58%, Sp = 93.43%, AUC = 0.935 DDSM: Acc = 87.27%, Sn = 82.5%, Sp = 90.33%, AUC = 0.920	MIAS DDSM
[32]	MRI	KNN	non-invasive lesion subtypeclassification	Acc = 74.7%, AUC = 0.816	Private 200 patients
[33]	US	SVM	discriminate benign and malignant tumors	Acc = 86.96%, Sn = 86.96%, Sp = 86.96%, AUC = 0.894	Private 138 cases
[34]	DM	SVM ANN	multiple classifier system for masses classification	SVM: AUC = 0.932 ANN: AUC = 0.925	DDSM 303 images
[35]	DM	SVM	detection of masses	Acc = 83.53%, Sn = 92.31%, Sp = 82.2%, AUC = 0.8033	DDSM
[36]	DM	RF	automated segmentation and classification method	Acc = 97.73%, Sn = 92.5% Sp = 98%, AUC = 0.9505	DDSM MIAS
[37]	DM	Fuzzy C-Means (FCM)	ROI classification into benign, malignant, or normal tissue.	Acc = 87%, Sn = 90 to 47%, Sp = 84 to 84%	DDM
[38]	DM	SVM	detection of microcalcifications (MC)	Sn = 92%, AUC = 0.8676	Inbreast 410 images
[39]	US	SVM	detection and diagnosis of breast masses	Acc = 95.85%, Sn = 96%, Sp = 91.46%, AUC = 0.9444	Private 120 images 70 benign 50 malignant
[40]	DM	SVM	classify feature vector as malignant or nonmalignant	IRMA: Sn = 99%, Sp = 99% DDSM: Sn = 97%, Sp = 96%	IRMA DDSM
[41]	US	SVM	evaluating breast tumors.	Acc = 96.67%, Sn = 96.67%, Sp = 96.67%, AUC = 0.9827	Private 210 images 120 benign 90 malignant
[42]	DM	SVM	Classification of breast cancer	Acc = 97.14%, Sn = 98.24%, Sp = 95.08%, AUC = 0.9938	WBC 699 cases 458 benign 241 malignant
[43]	DM	SVM	classification as malignant masses and benign tumors	Acc = 99%, AUC = 0.90	MIAS
[44]	MRI	SVM KNN RF	discriminating malignant and benign breast lesions.	SVM: Acc = 82.8%, Sn = 94%, Sp = 77.8%, AUC = 0.809	Private 234 training 93 test
[45]	MRI	Fuzzy C-Means (FCM)	detecting breast masses	Detection rate = 100%	Private 61 biopsy-lesions
[46]	IRT	ACO	classifying breast into benign and malignant cases	Acc = 79.52%	Private 146 images 29 malignant 117 benign
[47]	DM	Fuzzy C-Means (FCM)	microcalcifications cluster enhancement method	Private: Acc = 95%, Sn = 93% MIAS: Acc = 94%, Sn = 82%	private MIAS

(continued on next page)

Table 4 (*continued*)

Reference	Imaging modality	Machine learning technique	Scope	Evaluation results	Image data sets
[48]	DM	SVM	breast mass classification	AUC = 0.805 ± 0.012	DDSM 600 benign and 600 malignant
[49]	DM	DT	detection of breast cancer based on three types of decision tree classifiers	Acc = 97.51%, AUC = 0.99382	WBC 699 cases 458 benign 241 malignant
[50]	DM	ANN	detection and classification of breast cancer.	Acc = 97.66%, Sn = 98.65%, Sp = 95.82%, AUC = 0.993	WBC
[51]	US	LDA	distinguishing positive and negative lymph nodes.	AUC = 0.85	Private 90 patients
[52]	DM	SVM ANN	detect and classify masses	SVM: AUC = 0.937 ANN: AUC = 0.925	DDSM
[53]	US	Multiple-DA	classification of breast mass	invasive carcinomas: Acc = 88.4% noninvasive carcinomas: Acc = 80.6% Fibroadenomas: Acc = 86.0% Cysts: Acc = 84.1%	Private 363 images 65 training set 298 test set
[54]	MRI	SVM	diagnosis of non-mass-enhancing lesions.	AUC figures	Private 84 images 61 malignant 23 benign
[55]	DM	ANN KNN	detection of malignant masses and architectural distortions	true-positive fraction (TPF) = 0.620	Private 200 cases
[56]	DM	ANN	tissue density classification using local binary pattern	AUC = 0.79	Private 400 image
[57]	DM	Association rule mining (ARM)	benign–malignant classification	Acc = 98%, Sn = 97.4%, Sp = 98.6%	DDSM
[6]	DM	ARM	classify between normal and cancerous tissues	Sn = 96.5% Sp = 96.88%	DDSM
[58]	US	Binary-LR	classification of BI-RADS category 3 breast masses	Sn = 95%, Sp = 73%, AUC = 0.95	Private 69 masses 21 malignant 48 benign
[59]	MRI	NB-QDA (NQDA) SVM Fisher's LDA	classification of the challenging lesions	NQDA: AUC = 0.87	Private 63 patients
[60]	DM	local linear wavelet-ANN based firefly	classifying breast cancer tumor	Acc = 98.14%	WBC
[61]	DM	LLWNN based recursive least square (RLS)	breast cancer recognition	Acc = 97.2%	WBC
[62]	US DM	Probabilistic-ANN	discriminate between benign and malignant	Acc = 93.5%	
[63]	IRT	SVM	detecting breast cancer.	Acc = 88.10%, Sn = 85.71%,Sp = 90.48%	Private 50 images 25 normal 25 cancerous
[64]	DM	Swarm Optimization-ANN	detects the presence of microcalcification clusters.	MIAS: Sn = 95%, Sp = 92.3%, AUC = 0.9761 Private: Sn = 91%, Sp = 86.1%, AUC = 0.9138	MIAS Private
[65]	DM	Differential Evolution Optimized Wavelet-ANN	detection of tumor masses	Sn = 96.9%, Sp = 92.9%, AUC = 0.97843	MIAS
[66]	US	SVM	classify tumors into benign and malignant	Acc = 91.07%, AUC = 0.96	Private 168 cases 72 malignant 96 benign
[67]	DM	SVM	classify potential micro-calcifications	Acc = 100%	MIAS Private
[68]	DM	Kernel Self-optimization Fisher-DA	breast tissue density classification	Acc = 94.46%	MIAS
[69]	DM	SVM ANN	characterize breast lesions according to BI-RADS classes	SVM: Acc = 96.91%,AUC = 0.924 ANN: Acc = 97.14%, AUC = 0.933	Private 286 cases

(*continued on next page*)

Table 4 (*continued*)

Reference	Imaging modality	Machine learning technique	Scope	Evaluation results	Image data sets
[70]	US	SVM	categorize the breast masses to benign or malignant classes.	Acc = 95%, Sn = 90.91% Sp = 97.87%	Private 80 cases 33 malignant 47 benign
[71]	DM	Ensemble learning system consisting of (DT, SVM, and KNN)	classification of a suspicious mass as malignant or benign	Acc = 72%	DDSM

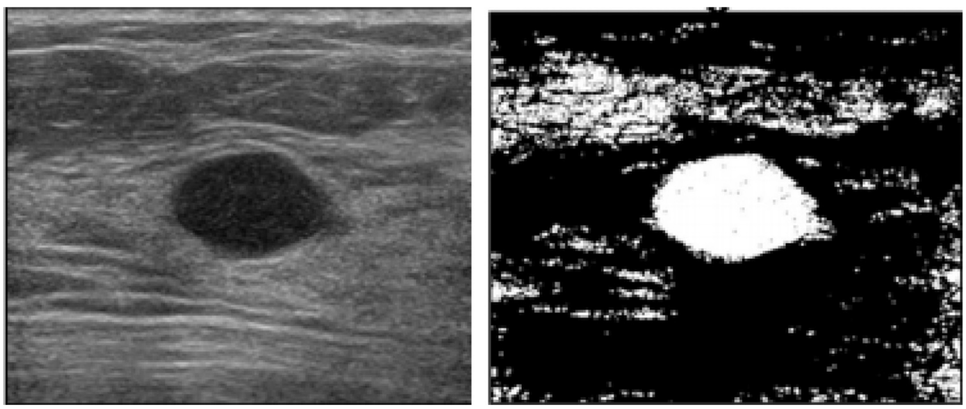

Fig. 4. Samples of US images used in publications of the proposed SR (adapted with permission from Elsevier Publisher from Ref. [72]) [72].

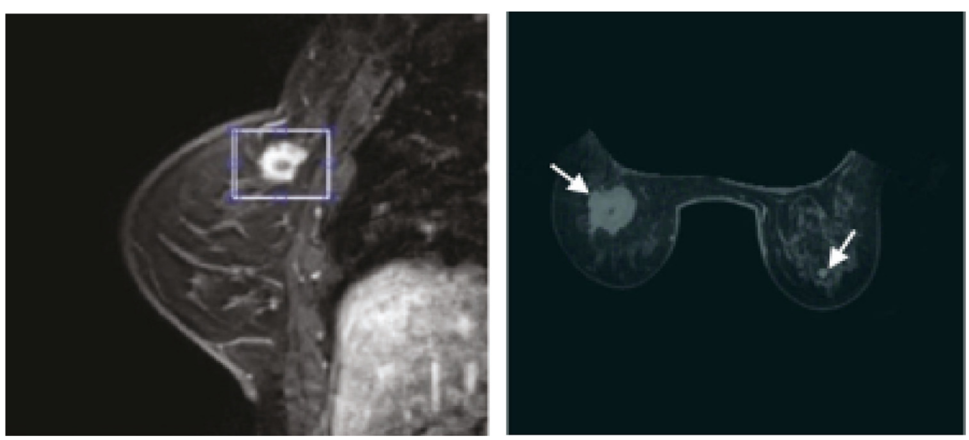

Fig. 5. Samples of MRI images used in publications of the proposed SR (adapted with permission from Springer Publisher from Refs. [44,45]) [44,45].

breast cancer are 30 papers. Fig. 4 presents samples of US images used in publications of the proposed SR.

MRI images the whole breast and presents it as thin slices that cover the entire breast volume; moreover, it provides information about the vascularity of the breast tissue. It shows high potential for screening of high-risk women, and evaluating therapy effects [179]. Only 14 papers mentioned in this SR use this type of modality. Fig. 5 presents samples of MRI images used in different publications of the proposed SR.

Microscopic images are using histological images which are *microscopic examinations* of tissues to detect tumors. Only 8 papers in this SR use microscopic images. Fig. 6 presents samples of microscopic images used in publications of the proposed SR.

IRT can be used in observing pre-cancerous and early signs of breast cancer using the temperature spectrum; tumorous cells have high temperature than healthy ones. Five papers included in this SR are using IRT. Fig. 7 presents samples of IRT images used in publications of the proposed SR. One of the considered papers used both of US and DM, so the total number of modalities in the chart is 155.

From data extraction process, Fig. 8 shows a pie chart of the used image modalities in the proposed literature papers. Each sector of the pie shows the extent of utilizing each of these different modalities. It is shown that the most used medical images for detection of breast cancer using CADs is the DM.

3.2. Selected features

The selected features are capable of differentiating between normal and cancerous regions in order to minimize the classification error. Different publications use different set of features which they found most suitable for this task. A huge number of features are assembled in this SR but only samples of the most used and selected features are presented in this section.

The most used features types which have been found in publications of this SR for breast cancer classification are histogram, morphological, textural, speculation, geometric, kinetic, and binary

Table 5
Science Direct (Elsevier) results.

Reference	Imaging modality	MLT	Scope	Evaluation results	Used data set
[72]	US	LR	classify breast tumors based on tumor size.	In data subset of tumors < 1 cm: Acc = 81.4%, Sn = 83.3%, Sp = 79.5%, AUC = 0.852 In data subset of tumors ≥ 1 cm: Acc = 81.8%, Sn = 85.4%, Sp = 77.8%, AUC = 0.855	Private 156 tumors 78 benign 78 malignant
[73]	DM	DL	detection of malignant lesions and benign abnormalities	AUC = 92.2%	Private 45,000 images
[74]	DM	QDA	automatic localization of malignant sites of asymmetry	Acc = 79%, Sn = 83%, Sp = 75%	MIAS DDSM 94 images
[75]	US	RF	Benign/malignant tumor classification	AUC = 99%	Private 31 malignant 28 benign
[76]	shear-wave elastography	DL	differentiation between benign and malignant breast tumors.	Acc = 93.4%,Sn = 88.6%, Sp = 97.1%, AUC = 0.947	Private 227 images 135 benign 92 malignant
[77]	DM	Extreme Learning Machine (ELM-ANN)	distinguishing malignant masses from benign ones	DDSM: Acc = 95.73, Sn = 94.88 Sp = 97.16, AUC = 0.9742 MIAS: Acc = 96.02%, Sn = 96.29% Sp = 94.32%, AUC = 0.9659	DDSM MIAS
[78]	DM	DL	diagnosis of breast cancer	Acc = 82.43%, Sn = 81% Sp = 72.26%, AUC = 0.8818	Private 1874 pairs of images
[79]	US	DT ANN RF SVM	distinguish benign from worrisome lesions	SVM: Acc = 77.7%, AUC = 0.84 RF: Acc = 78.5%, AUC = 0.83	Private 283 lesions
[80]	DM	ANN	classify tumors as benign or malignant	Acc = 90.94%, Sn = 100% Sp = 97.30%, AUC = 96.89%	MIAS 57 images 37 benign 20 malignant
[81]	DM	DT, DA KNN, NB Probabilistic-ANN SVM, AdaBoost Fuzzy Sugeno (FSC)	classification of normal, benign and malignant	KNN: Mean Acc = 98.69% Sn = 99.34%, Sp = 98.26%	DDSM 690 images
[82]	DM	ANN	online classification as normal benign/ malignant tumor.	Acc = 96% Sn = 98.6% Sp = 89.3%	MIAS BancoWeb 100 images
[83]	DM	ANN Neuro-fuzzy	mass detection process	BRBP-ANN: Average Recognition rate = 97.08% Neuro-fuzzy: average recognition rate = 95.42%	MIAS
[84]	DM	DL	breast mass classification	Acc = 96.7%	DDSM
[85]	DM	DL	classification of mass lesions	AUC = 0.826	Private 344 patients
[86]	DM	DT RF SVM PL	differentiating normal, benign and malignant in breast tissue	PL: Acc = 100% AUC = 1.00	DDSM BCDR
[87]	DM	ANN SVM	computer aided detection (CAD) systems	ANN: Acc = 79.1%,Sn = 81.6%, Sp = 71.1%	Private 400 cases
[88]	cytological images (microscopic Images)	ANN SVM	classification system for cancer malignancy grading	ANN: Acc = 87.1%,Sn = 100%, Sp = 86.4% SVM: Acc = 77.23%,Sn = 96.49%, Sp = 77.27%	Private 202 images in the database, 101 cases. Pair of images describes a single case
[89]	US	Binary-LR	computer-aided tumor detection	mapping rate of 80.39%	Private 18 cases
[90]	DM	SVM	classification as mass or normal and breast density classification	Mini-MIAS: Acc = 99%, AUC = 0.9325 Inbreast: Acc = 92.37%, AUC = 0.99	Mini-MIAS Inbreast
[91]	shear-wave elastography	LR	distinguish malignant from benign breast tumor	Acc = 88%, Sn = 81% Sp = 91% AUC = 0.89	Private 57 benign 31malignant

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Table 5 (*continued*)

Reference	Imaging modality	MLT	Scope	Evaluation results	Used data set
[92]	DM	SVM	automatic mass detection for diagnosis of suspicious regions	Sn = 82.4%	DDSM
[93]	DCE-MRI	LDA KNN Gentleboost (GB) SVM RF	detection of breast	RF: Sn = 95%	Private 209 images
[94]	US	SVM	automatically detect the tumor regions	Acc = 0.983 ± 0.013 Sn = 0.974 ± 0.035 Sp = 0.985 ± 0.019 AUC = 0.997 ± 0.003	Private 46 images
[95]	DM	AdaBoost	detection and classification as benign /malign	Mean Acc = 91.43% Sn = 87.15%, Sp = 93.58% AUC = 0.9036	MIAS
[96]	DM	KNN	distinguish between normal and abnormal breast tissues and tumors as malignant or benign	Mini-MIAS abnormality detection: Acc = 91.27, AUC = 0.989 malignancy detection: Acc = 81.35, AUC = 0.841	Mini-MIAS 252 images DDSM 11,553 ROI
[97]	DM	SVM	classification of regions extracted as mass /non-mass.	Acc = 98.88% Sn = 98.60% Sp = 98.85%	DDSM 3404 ROI
[98]	Elastography	Fuzzy C-means	distinguishing malignant from benign tumors	Acc = 80%, Sn = 80% Sp = 80%, AUC = 0.84	Private 45 malignant 45 benign
[99]	DM	SVM	distinguishing between abnormality (mass/ microcalcifications) &(benign/malignant)	Acc = 99% ± 0.50 AUC = 0.9900 ± 0.0050	MIAS Inbreast
[100]	DM	ANN	classification as(normal/abnormal) then the abnormal as (benign/malignant)	RBFNN(normal/abnormal): Acc = 93.98, Sn = 97.22% Sp = 91.49% RBFNN(benign/malignant): Acc = 94.29%, Sn = 100% Sp = 89.47%	MIAS
[101]	US	NB LR AdaBoost	differentiating benign and malignant masses	Sn = 90% sp = 97.5% AUC = 0.98	private 246 patients
[102]	US	SVM	lymph node classification	Sn = 95%, Sp = 90%, AUC = 95%	Private 105 images
[103]	US	Binary LR	second viewer to avoid misclassification of carcinomas.	Acc = 83%, Sn = 76%, Sp = 88%	Private 69
[104]	DM	SVM	predict the near-term risk of developing detectable high risk breast cancer in the next sequential screening mammography examination	AUC = 0.754 ± 0.024	Private 90 cases
[105]	DM	LDA	breast density classification	MIAS: Acc = 99.75 FFDM: Acc = 91.58%	MIAS 322 images Private full-field digital mammogram (FFDM) 1459 images
[106]	DM	SVM KNN DT Fisher LDA	classify as normal, benign, and malignant	SVM: Acc = 90.60%	DDSM IRMA MIAS
[107]	DM	Extreme Learning Machine (ELM-ANN)	breast tumor detection	Acc = 82.6% Sn = 86%, Sp = 78.9%	Private 482 images
[108]	DM	MLP-ANN KNN SVM	classify as normal/abnormal & benign/malignant	MLP-ANN: Acc = 71% Sn = 66% Sp = 77%	MIAS 181 images
[109]	DM	PL	define the mammogram images as normal or abnormal	AUC = 0.98 ± 0.03	DDSM 360 images
[110]	microscopic images	KNN NB DT	classify as benign/malignant	All classifiers: Acc = 96 to100%	Private 500 images 25 benign 25 malignant
[111]	DM	SVM	classification as mass or non-mass	Acc = 96.38%, Sn = 100% Sp = 95.34% AUC = 0.93	DDSM

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Table 5 (*continued*)

Reference	Imaging modality	MLT	Scope	Evaluation results	Used data set
[112]	DCE-MRI	LSMD LR SVM	differentiation between malignant and benign lesions	SVM: Sn = 95% Sp = 78.19% AUC = 0.9651–0.9755	Private 115 images 78 malignant 37benign
[113]	DM	SVM	predict the risk or likelihood of breast cancer development	AUC = 0.725 ± 0.018	Private 994 cases
[114]	MRI	SVM	classify into normal or non-normal	Acc = 98%	Private 120 images 70 normal 50 abnormal

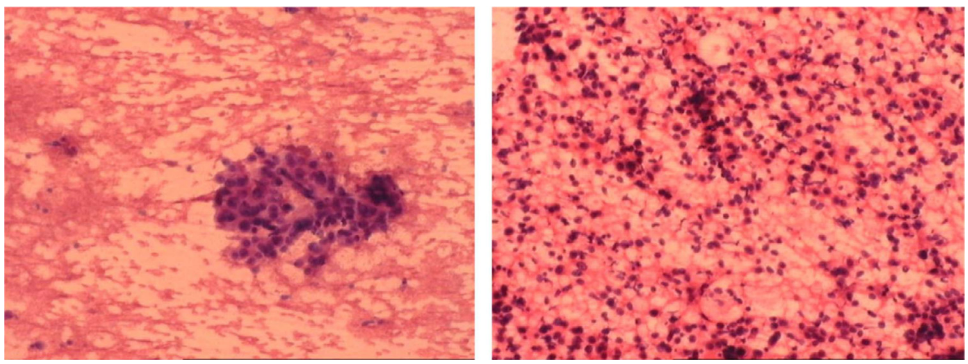

Fig. 6. Samples of histological images used in publications of the proposed SR (adapted with permission from Elsevier Publisher from Ref. [88]) [88].

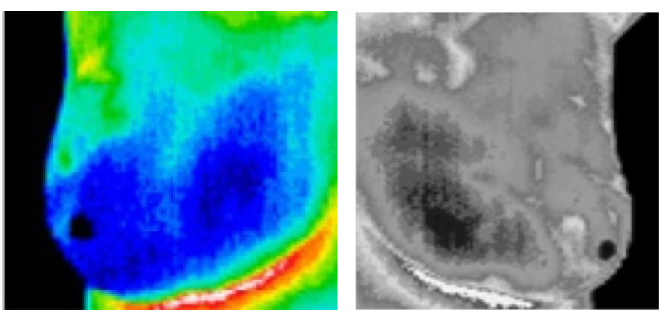

Fig. 7. Samples of IRT images used in publications of the proposed SR (adapted with permission from Springer Publisher from Ref. [63]) [63].

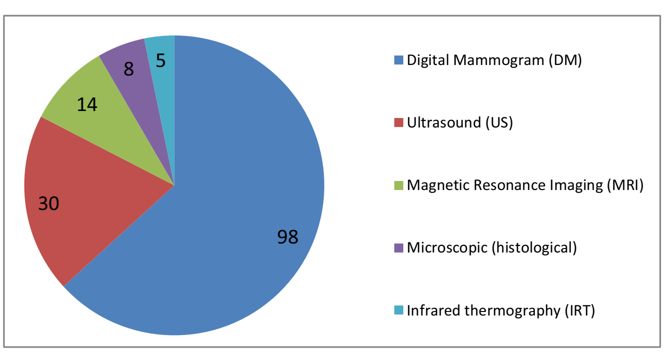

Fig. 8. Pie chart of different modalities used in different CAD systems.

object features. Samples of observed features for each of these different types are:

Histogram Features like Mean, Standard Deviation, Skew, Energy and Entropy.

Morphology like Area overlap ratio, normalized average radial distance ratio, standard deviation of normalized distance ratio, variance of distance ratio, compactness, smoothness, margin sharpness, variance in margin sharpness.

Textural like Contrast, Correlation, Difference in entropy, Difference in variance, Energy, Entropy, Homogeneity, Information measure of correlation, Maximum correlation coefficient, Sum average, Sum entropy, Sum variance, Variance, Inertia, Inverse difference

Spiculation like Margin sharpness, Full Width Half Maximum(FWHM) border, Variance in margin sharpness, FWHM grown, Radial gradient index, Radial gradient grown, Radial gradient border, FWHM ROI, Radial gradient ROI, FWHM margin, Radial gradient margin.

Geometric: Size, Circularity, Sphericity, Irregularity.

Kinetics: Maximum enhancement, Time to peak, Uptake rate, Washout rate, Curve shape index, Enhancement at first post contrast time point, Signal enhancement ratio.

Binary Object Features like Area, Centroid, Orientation (Axis of least second moment), Perimeter, Euler number, Projection, Thinness and Aspect ratio [166,167,169].

The selected features are always organized in a database and provided as an input to the MLT classifier.

3.3. Machine learning techniques

Several MLTs are used for breast cancer detection, prediction, and diagnosis. For the classification algorithms, the dataset is divided into training and test sets. Developing the model is done using the training dataset; afterwards the validation of the training model is accomplished using the test dataset. From data extraction process, many MLTs are used for the classification of breast tissues based on the features extracted from images.

In Tables 4–7, only the results obtained due to the test set examination are extracted. Some studies use more than one MLT classifier to find the best method in classification of different breast cancer problems, in this case only the best Acc values achieved for each problem are recorded such as in [28]. In papers that adopt one or more classifiers and use others for the purpose of comparison, only the adopted classifiers are mentioned. In

Table 6
IEEE search results.

Reference	Imaging modality	Machine learning technique	Scope	Evaluation results	Used data set
[115]	DM	DL	classification to mass and normal	Sn = 89.9%	Private 198 images (99 mass and 99 normal)
[116]	DM	SVM MIL	classification as normal or abnormal	MIL: AUC = 94.4%	DDSM
[117]	DM	SVM	Classification of breast cancer	Acc = 91.25%	(DDSM)
[118]	US	Back Propagation –ANN	Classification of breast cancer	Acc = 94.0% Sn = 94.4% Sp = 93.6%	Private 200 images 102 benign 98 malignant
[119]	DM	NB DT KNN SVM	classification of breast tumors	SVM: Acc = 74.92%	MIAS Inbreast
[120]	histopathology images (microscopic Images)	KNN SVM RF Quadratic Linear Analysis (QDA-LDA)	classification into two classes	QDA: Acc = 100%	Private 7909 images 82 patients
[121]	DM	Transductive Semi Supervised - SVM	classification of the tumors in terms of benignity or malignancy	Acc = 93.1% Sn = 83.0% Sp = 89%	DDSM 200 images
[122]	DM	SVM KNN	classification of tissue density	SVM: Acc = 91.51%, Sn = 87.33% Sp = 93.63%	MIAS
[123]	IRT	DT	classification of breast cancer	Acc = 90.10% Sn = 81.02% Sp = 92.35%	Private 150 images
[124]	DM	Optimum-Path RF	classification to identify the presence of breast masses	Recognition rate = 99.9%	Private 120 images
[125]	DM	SVM	classification of breast cancer	Acc = 96.3%, Sn = 98.7% Sp = 90.1%	MIAS
[126]	DM	ANN	classification of breast tissues into groups of normal and abnormal	Classification rate = 91.64%	MIAS
[127]	DM	SVM	classification of breast cancer	MIAS: Acc = 95.80%, Sn = 98.43% Sp = 93.34% DDSM: Acc = 95.78%, Sn = 96.74% Sp = 94.87%	MIAS DDSM
[128]	DM	SVM	classification of breast cancer	Acc = 94.44%, Sn = 95.88% Sp = 93.10%	DDSM
[129]	DM	Fisher's Linear-DA SVM, DT KNN	classification of breast cancer	SVM: Acc = 94.67%	IRMA
[130]	DM	SVM KNN DA	classification between masses and normal breast tissue	KNN: Sn = 94% Sp = 98%	DDSM
[131]	DM	Multiple-Instance Learning (MIL)	Classification to recognize benign versus cancer discrimination	Acc = 91.1%	DDSM 720 images
[132]	IRT	Fuzzy Classifier	classification between cancerous and healthy breasts	Sn = 82.35% Sp = 92.15%	Private
[133]	DM	ANN	classification of masses on a risk rate scale	Acc = 98%	Private 100 patients
[134]	DM	SVM	classification of breast cancer	Acc = 98.33%	Private
[135]	pathological images microscopic images	SVM	differentiating stage I breast cancer from other stages	Classification accuracy improved by 3%. Classification performance is 12%.	Publicly available database TCGA (The Cancer Genome Atlas). 86 patients
[136]	DM	Echo State Network (ESN-ANN) SVM	classification as malignant and benign cases	ESN-ANN: Acc = 98%	MIAS
[137]	Microscopic	SVM	classification of breast cancer	Classification efficiency = 82%.	Private
[138]	MRI	SVM	classification of suspicious malignancy	Acc = 94%	Private 70 clinical cases
[139]	DM	SVM	classify normal from abnormal cases	Acc = 96%	DDSM

(*continued on next page*)

Table 6 (*continued*)

Reference	Imaging modality	Machine learning technique	Scope	Evaluation results	Used data set
[140]	IRT	Sequential Minimum Optimization-SVM NB	classification for detection of malignant breast conditions	SMO-SVM: Acc = 61.8%, Sn = 61.72% Sp = 62.9%	Private 102 images 54 normal 48 finding
[141]	DM	Multi-Layer Perceptron (MLP-ANN)	classification between normal, benign, and malignant.	MLP-ANN: Acc = 96.66% Sn = 96.73% Sp = 97.35% AUC = 96.6%	Private 40 images 14 benign 6 malignant 20 normal
[142]	DM	(MLP-ANN)	classification into malignant, benign and normal cases.	Acc = 91.66%,Sn = 88.88% Sp = 93.72% AUC = 96.7%	private 40 images
[143]	US	Fuzzy-ANN	Classification of breast nodules as either benign or malignant	Acc = 90% to 92%	Private 65 images 31 benign 34 malignant
[144]	DM	Radial Basis Function-ANN	classification into benign and malignant masses	Acc = 89%, Sn = 89.5% Sp = 11.54%	Mini MIAS 148 images
[145]	DM	(MLP-ANN) SVM KNN	classification of breast cancer	AUC Figures	MIAS 80% training 20% testing.
[146]	DM	SVM	classification of breast cancer	SVM: Recognition rate = 89%	DDSM
[147]	US	SVM	classification of breast masses	Acc = 89.0 ± 3.6%, Sn = 91.0 ± 5.2%,Sp = 91.0 ± 6.6%	Private 200 images
[148]	DM	SVM	classification of breast cancer	Reduced FPs by 30% with the true detection rate at 85%.	Private 200 images
[149]	DM	SVM, NB KNN, LR DT, RF (MLP-ANN)	classification of breast cancer	SVM: Acc = 74% MLP: Acc = 76%	MIAS
[150]	US	SVM	classification of breast cancer	Acc = 88.18%, Sn = 88.33% Sp = 88.00%	Private 105 cases
[151]	DM	SVM	classification of breast masses	Acc = 89.09%	DDSM 600 training 200 test
[152]	DM	Adaptive Kernel Learning – NB	classification of breast cancer	Sn = 87%	Private 66 cases
[153]	DM	ANN SVM	classification of breast cancer	SVM: Sn = 98% at 0.85 FP/image ANN: Sn = 98% at 0.6 FP/image	MIAS
[154]	DM	Fuzzy Inference Systems (FIS) SVM	classification to detect micro calcifications	SVM: Sn = 99.60% Sp = 99.11%	MIAS 16 images

the papers that try many MLTs to classify breast cancer problems, all of them are mentioned and only the best achieved results are recorded in the data tables. In case of using combined MLTs, all of them are mentioned and Acc of the combined techniques are recorded.

A brief description of each technique used in the SR is given below:

SVM classifier is the widely used MLT in the papers investigated in our SR. It is a supervised classifier. It builds a model that uses a hyperplane as a boundary that distinguishes various points in 2 different classes and separates them. This plane is used to classify a test sample [180]. In the presented study, the number of publications which adopts SVM as a classifier is 81which represents 52.6% of the total considered studies. The maximum accuracy achieved using SVM is 100% as stated by [67]. Also, in [90] the Acc. value achieved by SVM is 99%. As can be seen, classifying breast cancer tissues using SVM can accomplish an excellent Acc values.

ANN classifier is a network that connects all nodes together imitating the human brain neurons. The input to one of the nodes is the sum of the output of all the nodes to which it is connected multiplied by a certain determined weight. A "transfer function" processes the output value from a certain node. The NN is formed of consecutive layers. An input layer receives data and transfers it to nodes in the first hidden layer after assigning them weights. The result is transformed to the nodes in the next layer and so on. The last layer provides the network's output. Number of ANN publications considered in the presented SR are 40 which is considered 25.97% from the total publications number. ANN has been combined with many other classification techniques such as: in [26], it is combined with associative classification technique which is called (ACNN) and with adding fuzzy it is called (ACFNN), this combination is created and evaluated. A fuzzy neural network is a single architecture combining the elements of fuzzy and neural network. It is a learning machine that uses the parameters as fuzzy sets. By using these techniques in combination with ANN, the authors indicate that the performance of ACFNN is better than ACNN with Acc equal to 95.1%. Also, the fuzzy inference system (FIS) is used with ANN as a neuro-fuzzy system in [83] with Acc 95.42%. Four considered papers are using wavelet neural networks (WNN) classifiers which is a kind of feed-forward network whose activation functions are drawn from wavelet basis such as [60] that has Acc of 98.14%. Five papers are using a multilayer perceptron (MLP) which is a feed-forward artificial neural network model that maps sets of input data onto a set of appropriate outputs. The Acc

Table 7
PubMed search results.

Reference	Imaging modality	Machine learning technique	Scope	Evaluation results	Used dataset
[155]	US	SVM	classification to tumor class	Acc = 98.2%, Sn = 98.4%, Sp = 97.8%	Private 110 cases
[156]	Histopathology (micro-scopic images)	DL	breast cancer detection	Breast results (mean ± std): Acc = 0.86 ± 0.03, Sn = 1, Sp = 0.72 ± 0.10	Private 58 H&E-stained histopathology images of breast tissue
[157]	DM	GentleBoost	Classify microcalcification groups	Sn = 76%, Sp = 98%	Private 1088 cases
[158]	DM	SVM NB KNN LR DT RF MLP – ANN	detection of mass	RF: Acc = 91.4%, Sn = 67.9%, Sp = 93%, AUC = 90.1%	mini-MIAS322 digitized mammograms
[159]	MRI	RF	differentiate among mass and non mass	Sn = 100%, Sp = 77%, AUC = 92%	Private 240 patients
[160]	US	SVM	distinguishing between TNBC and benign	Acc = 94.81%, Sn = 94.12%, Sp = 96.72%	Private 169 images
[161]	microscopic images	RF SVM	diagnosis of breast cancer	Acc = 90%, Sn = 94.59%, Sp = 96.72%	Private 228
[162]	DM	ANN	detection of breast cancer	Sn = 68.8%, Sp = 95%, AUC = 0.851 ± 0.046	Private 1896
[163]	US	SVM	discriminate the grades of breast cancer tumor	Acc = 85.14%, Sn = 79.31%, Sp = 86.55%	Private 148 images
[164]	DCE-MRI	SVM	classifying as malignant and benign	Sn = 80.0%, Sp = 90%, AUC = 0.919 ± 0.029	Private 115 images
[165]	DM	AdaBoost-SVM	diagnosis of breast cancer	AUC = 0.89	DDSM
[166]	DM	Fully Complex-Valued Relaxation Neural Networks (FCRN) ANN	classification as normal, benign and malignant	Acc = 98, Sn = 97, Sp = 100, AUC = 0.947	MIAS
[167]	DCE-MRI	SVM	discriminate between lesion classes	AUC = 0.77	Private 585 cases
[168]	MRI	fuzzy c-means	distinguishing malignant and benign lesions	AUC = 0.88	Private 15 malignant and 8 benign
[169]	MRI	Bayesian ANN	classification of breast cancer using HiSS MRI and clinical DCE-MRI	For HiSS AUC = 0.92 ± 0.06 For DCE-MRI AUC = 0.90 ± 0.05	Private 40 cases with 34 malignant, 7 benign lesions
[170]	microscopic images	KNN ANN SVM	classification into different grades of malignancy (grades I–III)	SVM ACC = 96.9	Private 65 ROIs: 20 grade I, 20 grade II, and 25 grade III.
[171]	DM	QDA	detection of breast diseases at their early stages	SN = 80% AUC = 0.70.	Private 158 images
[172]	DM	DT LDA SVM	classify breast cancer as normal, benign, and malignant	DT: private DB Acc = 96.3% DDSM Acc = 91.6%	Private 300 images DDSM 300 images
[173]	US	DT	classify breast cancer	AUC = 0.90 ± 0.03	Private 250 patients 96 malignant 154 benign
[174]	DM	SVM	detection of suspicious lesions in mammogram	Sn = 94.5%	MIAS 164 images
[175]	DM	LR	classify breast cancer	AUC = 0.7838	DDSM Private (1006 cases (646 benign and 360 malignant))
[176]	US	SVM	classifying solid breast masses	ACC = 75.5, Sn = 78.9%, Sp = 73.6%, AUC = 0.82	private 110 images

achieved using MLP in [141] is 96.66%. Many other types of ANN have been used in the literature such as probabilistic ANN, radial basis function (RBF), extreme learning machine (ELM), and convolutional ANN or CNN which is used in deep learning.

KNN classifier is a supervised classification method. It classifies an unknown sample by initially calculating the distance of that sample to all the training samples. It determines k smallest distances. The output class label of the unknown sample is assigned by the most represented class in these k classes. The number of KNN publications considered in the presented SR is 21 which is considered 13.63% from the total publication number. Many MLTs were used in [81], KNN is the classifier which achieved the highest recorded mean Acc, that is 98.69%.

DT sets a series of carefully composed questions about the attributes of the test record in a tree structure. Every time an answer is received, a follow-up question is asked till a conclusion is driven about labeling the class of the record. A decision tree classifier is composed of one root node, several internal nodes, and several terminal nodes. The root and internal nodes include the test conditions for the attributes to distinguish between records that have different qualities. All terminal nodes are assigned a class label. For building decision trees the core algorithm uses entropy to evaluate how homogenous the sample is. If homogeneity is fully satisfied the entropy is zero and if the sample is an equally divided it has entropy of one. Decision tree construction is about finding an attribute that returns the highest information gain or in other words that returns the most homogeneous branch. The information gain is based on the decrease in entropy after the splitting of a dataset based on a certain attribute. The number of DT publications considered in the presented SR is 14 which is considered 9% from the total publication number. The highest Acc value achieved using DT is 97.51% in [49].

DA is a statistical supervised classifier that aims to find decision functions that respond to samples from different classes in a different manner. Three types of DA are collected in the presented SR which are Linear (LDA), Quadratic (QDA), and Kernel. All types of DA are counted together; the number of DA publications considered in the presented SR is 14 which is considered 9% from the total publication number. The highest Acc value achieved using kernel self optimization fisher DA is 94.46% in [68].

RF merges several decision trees for prediction, and they are constructed by grabbing several classification trees together. Each one of these trees is an independent one. When data is extremely unbalanced the RF gives suboptimal results. RF can be implemented easily and it performs predictions for large number of input variables with high accuracy. The number of RF publications considered in the presented SR is 13 which is considered 8.4% of the total publication number. Using RF in [124] achieved maximum Acc of 99.9%.

Fuzzy classifier specifies partial membership for an object in different classes with different degrees. A classifier is described by fuzzy IF-THEN rules. Fuzzy c-mean (FCM) is the most popular unsupervised classification algorithm based on fuzzy. In this case, the data points have their membership values with the cluster centers, which will be updated iteratively. Twelve papers are using fuzzy classifiers which are considered 7.79%. In [45] the achieved Acc is 100% using fuzzy.

NB depends on a probabilistic technique and Bayes theorem. It gives probabilities that a given pattern belongs to a specific class. The probability of a random class variable is measured and computed from observations that are given about the value of another set of random variables. There are 10 NB classifiers found in the collected studies which are considered 6.4%. NB achieved Acc ranges from 96 to 100% as stated in [110] for all used classifiers.

LR was developed by statisticians and it is commonly used in learning as other classifiers developed by the ML scientists. LR is mostly used for binary classification problems. It predicts the probability of an incident based on a set of values used as predictors. In this SR, 10 publications adopt LR as a classifier which is considered 6.4%. The maximum Acc recorded using LR is 88% in [91].

DL recent trend in machine learning resulted in new techniques to train deep neural networks, which produce highly successful applications in many pattern recognition tasks such as image and speech recognition [73]. So the most publications found in this SR that uses DL are recent ones. DL is a set of algorithms that try to learn in multiple levels, representing various levels of abstraction. DL typically uses ANN. Distinct levels of concepts are represented by the levels in the learned statistical models. Concepts of higher level are defined from lower-level ones, and at the same time these lower level ones can help to define other higher-level concepts. DL uses the back propagation algorithm to find out complicated structure in huge data sets to indicate how a machine should change its internal parameters that are used to compute the representation in each layer from the representation in the previous layer [181,182]. The maximum Acc recorded using DL is 96.7% in [84].

Ensemble system is a combination of optimized classifiers whose output was combined using ensemble combination rules like majority voting, minimum, maximum, average and product. A few number of ensemble systems are found in our SR. One of them consists of (DT, SVM, and KNN) and its achieved Acc was 72% [71]. It is observed that using standalone classifier achieve greater Acc value than when it is used in ensemble system. Also, four boosting learning are found in data extraction. Boosting is an ensemble machine learning method which converts weak learners to strong ones. The used boosting algorithms are Adaptive Boosting (AdaBoost), and Gentleboost. In [95], the achieved mean Acc using AdaBoost is 91.43%. In general, using ensemble algorithms in breast cancer CADs is considerably little which can be a point of research in the future to improve the performance of CAD systems for better cancer diagnosis.

ARM is used for discovering the repeated items, correlations, or associations in different datasets and thus generates the association rules between sets of items. Three papers uses ARM with achieved Acc 98% in [57].

MIL is a supervised learning that solves learning problems with incomplete information about data labels. In MIL, each instance is described by a feature vector and the class label is associated with a big bunch of instances. The aim of the MIL is to develop learning model for these bunches classification. Two articles have used MIL as a classifier [131] and [116] the first one achieved Acc of 91.1% and the second obtained AUC of 94.4%.

PL maps a d-dimensional feature vector into an L-dimensional vector. Therefore, the dimensionality of the expanded vector can be expressed in terms of the polynomial order and the dimensionality of the input vector. Finally, the classifier output is obtained after a linear combination of the expanded vector. Two papers are using PL to classify breast cancer tissues. 100% Acc value has been obtained in [86].

Each of the following MLTs have been used in one article:

ACO is used for classification using an Ant-Miner algorithm. It is built on performing classification using a rule base that is to be optimized using ant colony optimization. [46] uses ACO and obtains a little Acc value of 79.52%.

LSMD uses a classification rule that calculates the minimum Euclidean distance between the unknown item and the mean values of each of the other classes, using a linear equation that minimizes the least square errors [112].

The obtained MLTs data have been analyzed using pie chart to find the most prominent technique used in CAD of breast cancer as declared in Fig. 9. It is noticed that SVM is the most used classification techniques for breast cancer CADs, and then ANN and K-NN

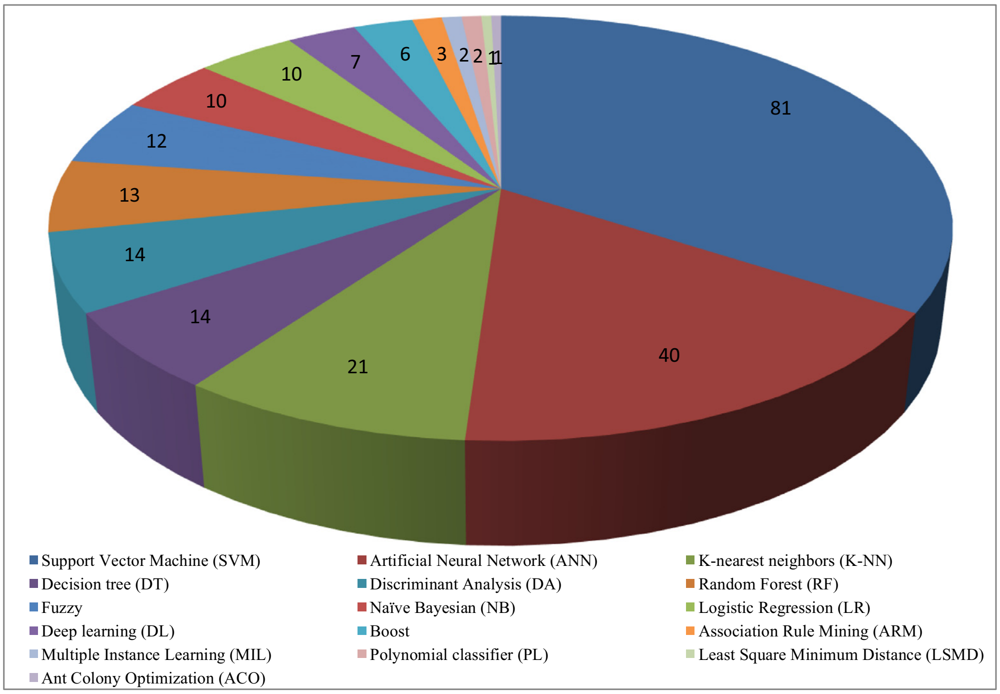

Fig. 9. Pie chart of the various MLTs used in CAD of breast cancer.

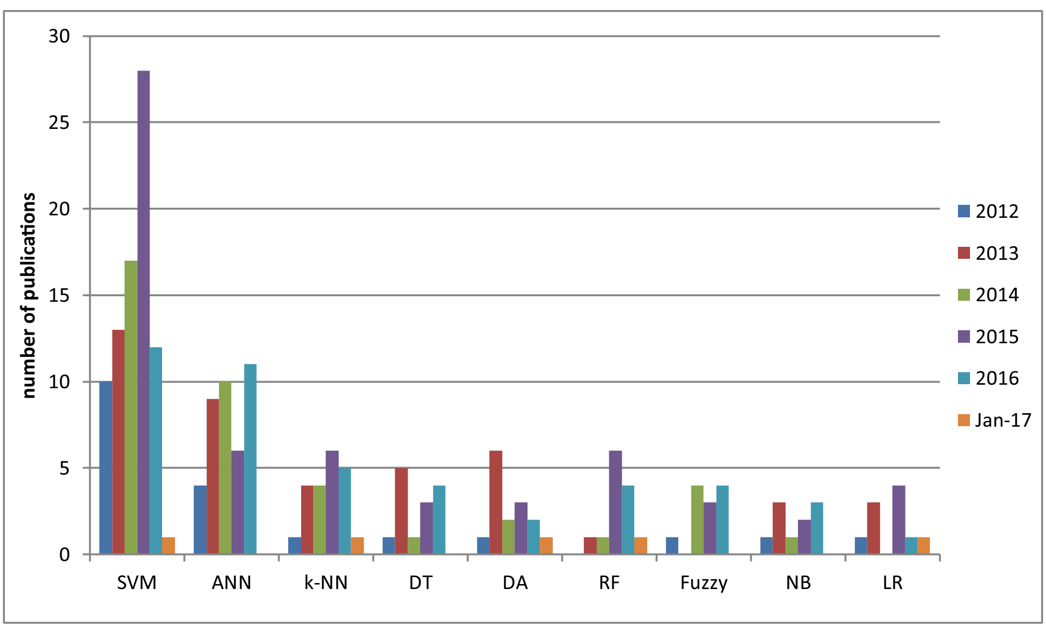

Fig. 10. Bar chart of the most commonly used MLTs in CAD of breast cancer per year.

come afterwards. Other techniques have been explored but have not been widely adopted.

Moreover, Fig. 10 presents the number of publications using a certain MLT for a specified year. The first 9 MLTs most commonly used for breast cancer CAD systems were plotted versus the years considered for this study; 2012 till January 2017.

3.4. Evaluation metrics

When a classifier is being trained using training data samples, test data are then fed to the classifier to be classified to assess the performance of the classifier. From data extraction process, it can be stated that there are several ways for assessing classifiers. In the evaluation process, the positive samples are those which go under the main class of interest. For cancer diagnosis, the positive samples are those of malignant/abnormal class and the negative samples are those of the benign/normal class.

The main and most used evaluation metrics applied to CAD systems include Acc, Sn, Sp, and AUC. These are the most repeated performance measures which are clearly mentioned in the selected articles. The articles which use other performance measures are not omitted to maximize utilization. However, only the popular metrics are defined as follows: (1) Acc represents how near the predicted class is to the actual one. That's to say it indicates percentage of samples that are rightly classified (normal and abnormal) to the total samples. (2) Sn is the true positive rate that determines the percentage of correctly classified abnormal samples. (3) Sp is the true negative rate which determines the percentage of correctly classified normal samples. (4) AUC is a common metric that represents a way to choose optimal models and ignore sub optimal ones. It is the area under the Receiver Operating Characteristic curve (ROC), which is a curve of the true positive rate versus the false positive rate. The AUC takes a value between 0 and 1. A good diagnostic test is obtained when the AUC is close to one. Reasonable tests have AUC greater than or equal to 0.5 and less than 1 [16].

Equations of Acc, Sn, and Sp are given as follows:

$$\mathrm{Acc} = \frac{\mathrm{TP}+\mathrm{TN}}{\mathrm{TP}+\mathrm{TN}+\mathrm{FP}+\mathrm{FN}},\ \mathrm{Sn} = \frac{\mathrm{TP}}{\mathrm{TP}+\mathrm{FN}},\ \mathrm{Sp} = \frac{\mathrm{TN}}{\mathrm{TN}+\mathrm{FP}}$$

where TP: true positive, TN: true negative, FP: false positive, FN: false negative.

3.5. Databases

Some public image databases are widely used for applying breast cancer classification methods. These databases are mostly DM images such as Digital Database for Screening Mammography (DDSM) [183], Mammographic Image Analysis Society (MIAS) [184], Image Retrieval in Medical Applications (IRMA) [185], Wisconsin Breast Cancer (WBC), and BancoWeb [186]. Also, there are two Portuguese's datasets, the first is the INbreast database [187] and the second is Breast Cancer Digital Repository (BCDR) [188].

Moreover, papers using other types of image modalities usually depend on private databases for applying their methods. Private databases are collected by individual groups independent of each other. Private databases present images of patients case studies collected in local hospitals or research centers. This holds back the analysis and comparison of different algorithms developed by one research group with the others and makes it ineffective. It is recommended to have standardized datasets that contain images from multiple sources for different image modalities.

In data extraction process, the used datasets in each article are collected as well as the number of images, patients, and cases as stated in the article. Also, the distribution of the datasets as (training and testing), (benign and malignant), and (normal and abnormal) is gathered. There is no standard neither in the number of cases used nor in the division of cases into benign and malignant or into normal and abnormal. So, there is a variety in the distribution of the data according to the insight of each author.

4. Discussion

It is noticed that there is a significant diversity in the usage patterns of MLTs, some of them have been used extensively, some have been used less frequently, and others have been used in low rates. Fig. 11 presents a hierarchy chart of MLTs categorized according to frequency of usage in CAD systems for breast cancer according to the studied articles.

A conclusion can be extracted from the studied articles according to the used image modalities combined with different MLTs as follows:

DM has been used with SVM in 50 papers; the range of achieved Acc is from 64.7% to 100%. Two papers have achieved Acc 100% and 19 papers achieved accuracy in range 90% - 99.5%. US has been used with SVM in 14 papers, the Acc ranges from 75.5% to 98.3%. Also, 9 papers are using MRI combined with SVM with maximum Acc value of 98% and the least achieved Acc was 82.8%. And 6 papers used microscope-SVM and the Acc registered is 96.9%. Only 2 papers are using IRT-SVM and the achieved Acc were 88.1% and 61.8%.

ANN is used with DM, US, MRI and microscopic images; it is used with DM in 34 papers and with US in 4 papers, one of them

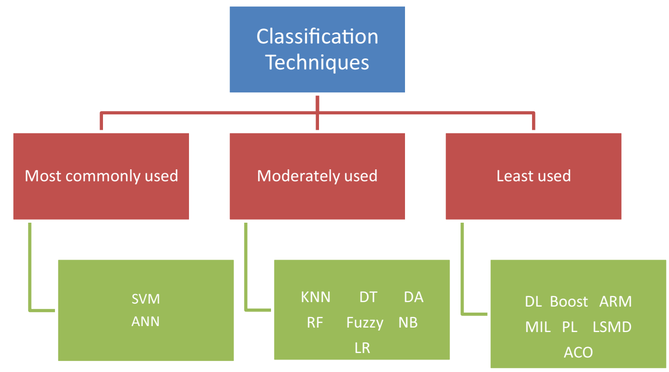

Fig. 11. Classification techniques categorized according to frequency of usage in CAD systems for breast cancer.

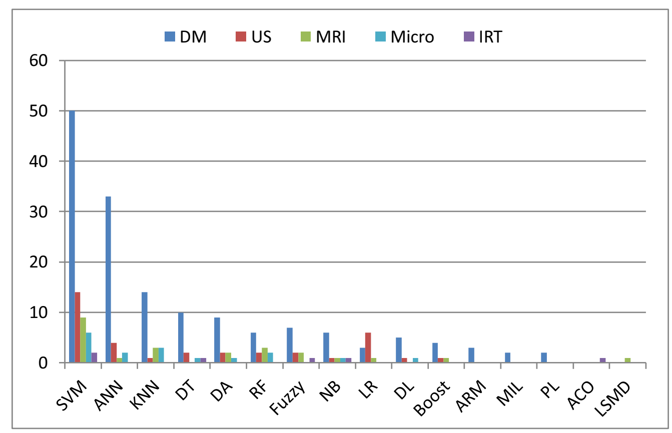

Fig. 12. The number of used MLTs with different modalities.

used both DM and US, only one paper with MRI and 2 papers with microscopic. In 20 papers with DM-ANN the Acc ranges from 90% to 98.14%. In the rest of the papers that stated the Acc values, its value ranges from 71% to 89.38%. The highest achieved Acc with US-ANN is 94%.

KNN has been used in 21 papers, 14 with DM with the highest Acc registered 98.69%. One publication combined KNN with US, 3 combined with MRI, and 3 combined it with microscopic modality. Table 8 shows the number of used MLTs distributed on different modalities and the highest registered Acc of each combination. Fig. 12 shows the number of used MLTs versus different modalities.

5. Conclusions and future work

This systematic review aims to help researchers in innovating and developing CAD systems to assist the medical society in detection/diagnosis and early treatment of breast cancer. The state-of-the-art of the MLTs that have been used for CAD to detect breast cancer from different image modalities has been explored. According to the collected data, it is difficult to comprehensively compare methods with each other due to several factors. Some of these factors are: the databases used for assessment, the samples of images selected for assessment, the number of samples used, the assessment approach (validation methodology, training and testing set) used. Moreover, the tuning of parameters involved in different methods varies from one method to the other, thus adding another obstacle for fair comparison between various methods. Generally, among the classifiers mentioned in the literature, SVM classifier has been used extensively for breast tissue classification purposes. The usage of artificial intelligence methods is increasing because

Table 8
The number of used MLTs with different modalities and the highest achieved Acc.

Total	SVM	ANN	KNN	DT	DA	RF	fuzzy	NB	LR	DL	boost	ARM	MIL	PL	ACO	LSMD
DM	50	33	14	10	9	6	7	6	3	5	4	3	2	2		
	100%	98.14%	98.69%	97.51%	99.75%	99.9%	95.11%	89.3%	–	96.7%	91.43%	98%	91.1%	100%		
US	14	4	1	2	2	2	2	1	6	1	1					
	98.3%	94%	–	–	88.4%	78.5%	90–92	–	88%	93.4%	–					
MRI	9	1	3		2	3	2	1	1		1					1/–
	98%	–	74.4%		–	–	100%	–	–		–					–
micro	6	2	3	1	1	2		1		1						
	96.9%	87.1%	96–100%	96–100%	100%	90%		96–100%	–	86%						
IRT	2			1			1	1							1	
	88.1%			90.1%			–	–							79.52%	

of the effectiveness in classification and detection schemes assisting experts in the medical field.

Clinically, in countries that are routinely using CAD, there is disagreement over the feasibility of using it as a result of some problems such as time and cost increase due to false positive and lack of training that lead to ignore suspicious lesions. Otherwise, in other countries, it is truly challenging to bring CADs into clinics by persuading the physicians with the effect of CADs as a supporting tool to improve physicians' performance. If some requirements are fulfilled then the CAD system may become widely applied in clinical practices without quarrel. These requirements are that the CAD should save the radiologists and physicians time and effort, and it should be affordable. Advances in CADs systems are to be obtained by their application and trial in clinics. Observing the pitfalls during the CADs clinical application will lead to improving their performance, thus reducing false positive that may lead to psychological, physical, and economic costs, and reducing false negative readings that may cause neglecting of treatment.

In the future work, it is recommended to have standardized public image databases that contain images from different image modalities for the same case to support the dependency of more than one image modality in classification task and combine information from multiple views. It will be wealthy if they contain DNA sequence of cases. This will enable CADs to provide results that depend on different perspectives concerning different modalities and even sequences.

Moreover, deep learning classifier is a promising trend that appeared in the recent years. There is an increased interest in applying it in CADs systems in the last couple of years. Also swarm intelligence is worth studying as it was rarely applied in the investigated publication in CADs systems. Developing MLT-CAD system that combines more than one image modality is a necessity. Also developing CAD systems using 3D mammography which is a new trend that may help to improve CAD efficiency is an important issue. These points should be considered to develop CAD systems in the future.

Conflict of interest

The authors have no conflict of interests to declare.

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