

REVIEW ARTICLE



Breast Cancer Segmentation in Mammogram Using Artificial Intelligence and Image Processing: A Systematic Review



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Abstract: **Background:** Breast cancer is the second leading cause of death in females worldwide. Mammograms are useful in early cancer diagnosis as well when the patient can sense symptoms or they become observable. Inspection of mammograms in search of breast tumors is a difficult task that radiologists must carry out frequently.

Objective: This paper provides a summary of possible strategies used in automated systems for a mammogram, especially focusing on segmentation techniques used for cancer localization in mammograms.

Methods: This article is intended to present a brief overview for nonexperts and beginners in this field. It starts with an overview of the mammograms, public and private available datasets, image processing techniques used for a mammogram and cancer classification followed by cancer segmentation using the machine and deep learning techniques.

Conclusion: The approaches used in these stages are summarized, and their advantages and disadvantages with possible future research directions are discussed. In the future, we will train a model of medical images that can be used for transfer learning in mammograms.

Keywords: Breast cancer, mammogram, cancer segmentation, deep learning, image processing, masses, benign.

1. INTRODUCTION

Out-of-control growth of breast cells causes Breast Cancer (BC), which is the second leading cause of death from cancer among women in the World, as shown in Fig. (1) [1, 2]. It is estimated that one in eight women will develop breast cancer during their lives. According to the World Health Organization (WHO) agency for cancer research, BC accounts for 2.1 million new cases and 627,000 deaths recorded among women in 2018 [3, 4]. In addition, WHO predicts the incidence of cancer will increase to 27.5 million by 2040, with an additional 16.3 million cancer deaths [5]. Risk factors for breast cancer include age, hormonal factors, smoking, early menarche, late menopause, family history, prior breast biopsy, diet and obesity, and socioeconomic status. Older women have higher chances of developing BC, as shown in Fig. (2). Successful treatment of breast cancer is possible through early diagnosis. Cancer leads to the uncontrollable reproduction of cells, which forms clusters of cells in a particular organ of the body. These clusters then form a lump, architectural distortion, and microcalcification, which creates tumors in the body. It is important to develop effective

methods for detecting the earliest signs of breast cancer for risk prevention. Different imaging tools are available for breast cancer screening and diagnosis, the most important of which are discussed in Table 1 along with their advantages and drawbacks. A mammogram is a low-dose X-ray of a breast to visualize the inner breast structures. It is one of the most common and latest approaches for identifying breast cancer early, which aids the radiologist and boosts the survival rate and treatment options. Accurate detection and segmentation of breast cancer are highly based on mammography. False-positive and false-negative diagnoses can result in useless procedures and in delayed diagnosis respectively. Radiologist performance may be improved with the development of technology-driven and workflow solutions. The mortality rate due to breast cancer can be reduced with the help of better diagnostic abilities and effective cures.

1.1. Computer-Aided Diagnosis (CAD)

CAD systems for mammograms are widely used to assist radiologists. According to the studies radiologists have an error rate between 10 to 30% in the detection of cancer [6, 7]. Sometimes radiologists miss out on major clues and become exhausted while manual screening mammograms. CAD systems are used to decrease the efforts required for the evaluation of cancer detection in clinical practices. The

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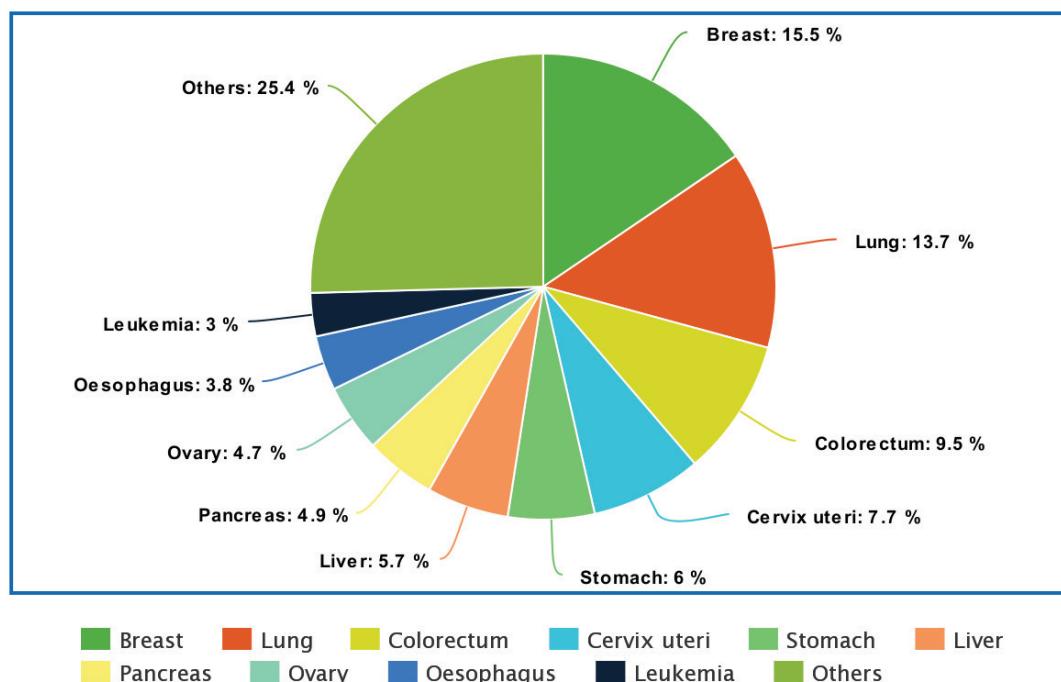


Fig. (1). Percentage of most common cancer in females, 2020. Source: GLOBOCAN 2020. (*A higher resolution / colour version of this figure is available in the electronic copy of the article.*)

benefits of utilizing developed breast cancer diagnostics systems include i) Aiding radiologists in the interpreting and evaluation phase as a second translator after a radiologist; ii) Decreasing the number of false positives thereby removing the need for unwanted biopsies and contributing to cost savings, and iii) Computer-assisted methods increase the accuracy of diagnosis by reducing false positives; iv) Minimizing patient's examination time by evaluating and recording the results in a few seconds, and v) Decrease radiologists workload without compromising quality in screening mammography.

A few papers were published to survey the methods used to diagnose cancer in mammographic images as discussed in Table 2 [8-13]. In this study, we discussed the latest research on the identification of breast cancer using image processing, traditional Machine Learning (ML), and Deep Learning (DL) techniques. The motto of this systematic review is to give the reader an insight into the literature on breast cancer and highlight the challenges of applying deep learning to early detection and recent developments in the detection of breast cancer using mammograms. We presented new studies discussing these problems, and eventually have some perspectives and debates on existing open challenges; moreover, the organization of the paper is shown in Fig. (3).

Research materials and methods are discussed in Section 2. In Section 3, we present a pipeline for the automated CAD system; public and private datasets, and preprocessing techniques used for mammograms are discussed in detail. Section 3.3 gives a comprehensive literature review of cancer segmentation techniques in mammograms using image processing, ML, and DL techniques. Mammogram classification techniques and evaluation methods used for the CAD system are discussed in Sections 3.4 and 3.5, respectively. Section 4

is about the discussion drawn from this paper, the issue presented in the literature, their possible solution, and future work. Section 5 presents the conclusion of this survey.

2. MATERIALS AND METHODS

The search strategy was carried out by searching through IEEE, Springer, PubMed, ScienceDirect, and Gray Literature databases such as Medical Literature Review and Retrieval System Online (MEDLINE) for related publications from 2002 to 2020 (including Google Scholar, papers published in conferences and journals, government technical studies, and several other materials regulated by hospitals).

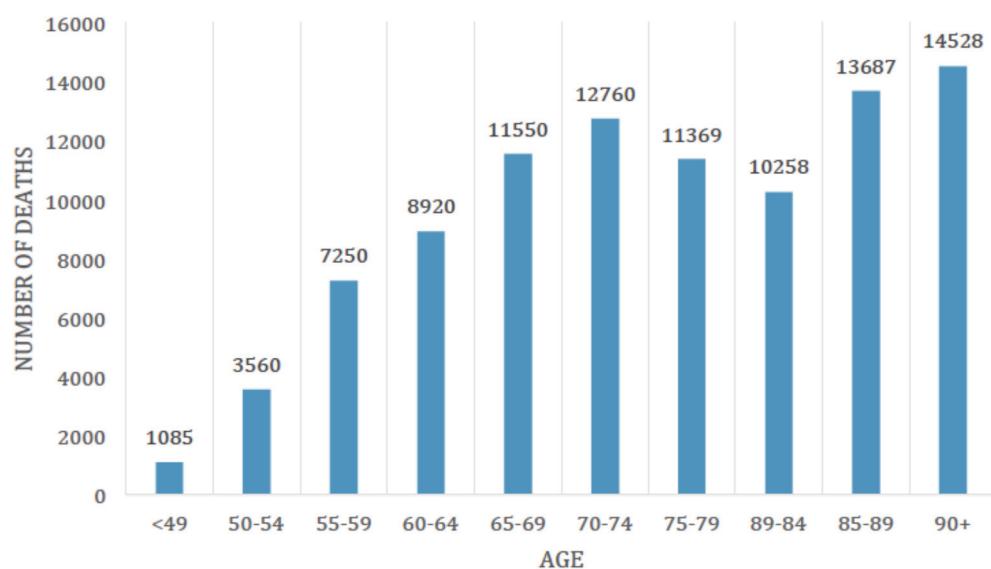
Mesh-based keyword searches included 'breast cancer', 'mammogram', 'deep learning', 'breast cancer screening modalities', 'classification models for mammograms', 'artificial intelligence techniques', 'segmentation models for mammograms', 'image processing techniques for mammogram cancer localization', and 'medical imaging'. We used the symbol "*" to retrieve all variations in the combination of logical relations such as "AND", "OR" and "NOT".

The selected papers were analyzed concerning the methods used in it, the nature of the image, the pros and cons of methods, the number of used features, and the results of the implementation methods. We provided the results in tabular form. Articles other than the English language are neglected in the searched articles. In addition, articles that did not have complete text were also omitted. All potentially applicable studies were independently reviewed by two experts. Disagreements were overcome by conversation by using a third expert's point of view.

Fig. (4) demonstrates the number of papers published each year for mammogram preprocessing, classification, and

Table 1. Various imaging techniques in breast cancer.

S. No.	Screening Modality	Recommended Age for Screening	Recommended Time for Screening	Use	Advantages	Disadvantages
1	Breast self-examination	20 years and older	Every month	Regular checkup	Anyone can perform on her own. This procedure is inexpensive and noninvasive.	—
2	Clinical breast exam	30 – 40 years	Every 3 year	Diagnosis	If any family history then it's better to go to the clinic for a regular checkup.	—
3	Mammograms	40 years and older	Every year	Screening and diagnosis	Low dose X-rays. Sensitivity is 90% for fatty breasts. Early detection is possible even before it can be felt by patients. It's also low cost.	Sensitivity is poor for a dense breast. The cancer missing rate is 25% in mammograms due to low intensity. Cancer detection is hard if the patient may have a dense breast.
4	Ultrasound	All ages	Depending upon the medical condition	Screening and diagnosis	Appropriate when the breast is denser. Widespread and effective supplement to mammography. Can discriminate between solid and cystic lesions.	Image accuracy and its interpretation is based on the person involved in the scan. Unable to detect cancer less than 1mm diameter.
5	Magnetic Resonance Imaging (MRI)	Upon medical request	-	Diagnosis	The sensitivity of MRI is approximately 99% for breast cancer detection. Recommended to the patients having breast cancer as a/the family history.	10 times the cost compared to mammography.
6	Biopsies	If cancer diagnosed	-	Treatment	Image-guided breast biopsy performed with MRI or Ultrasound support. While core biopsy provides quicker clinical outcomes than surgical excision.	The treatment process is invasive, and the patient may suffer from breast pain, stress, swelling, weariness, and skin desquamation.

**Fig. (2).** Estimated Number of deaths among women according to age group, 2016-2020. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

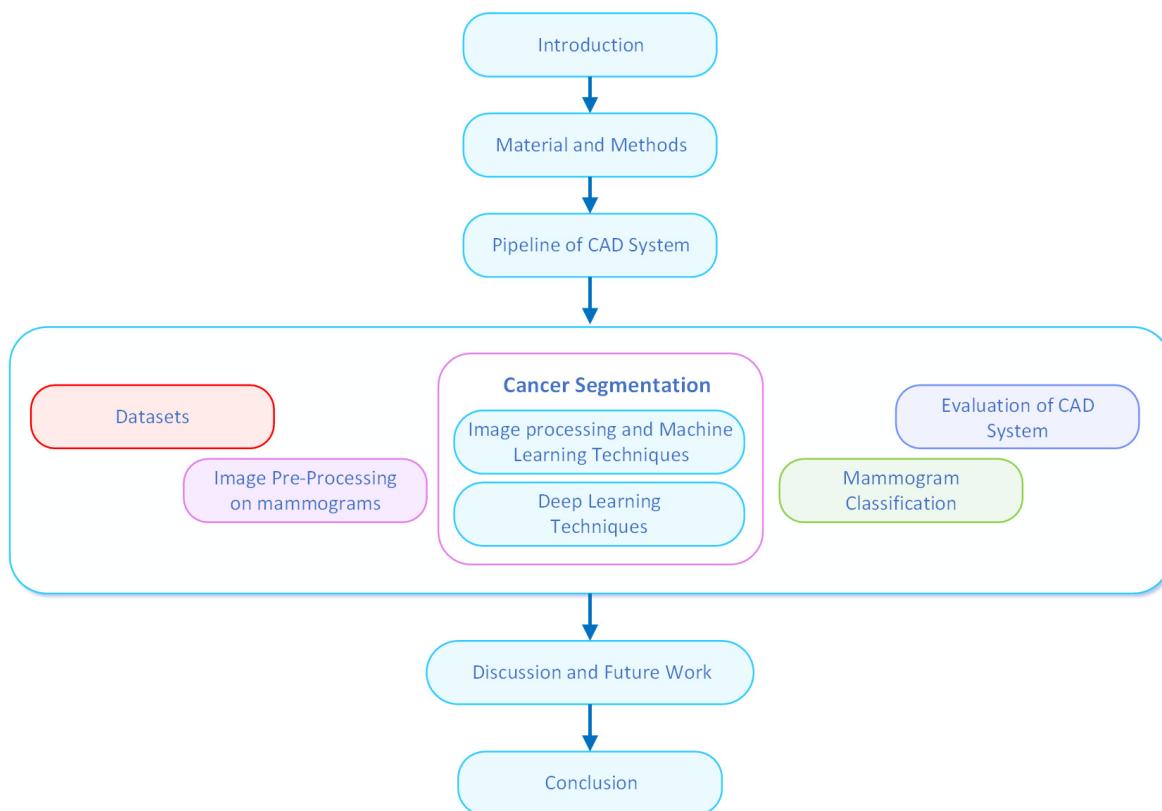


Fig. (3). Organization of the paper. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

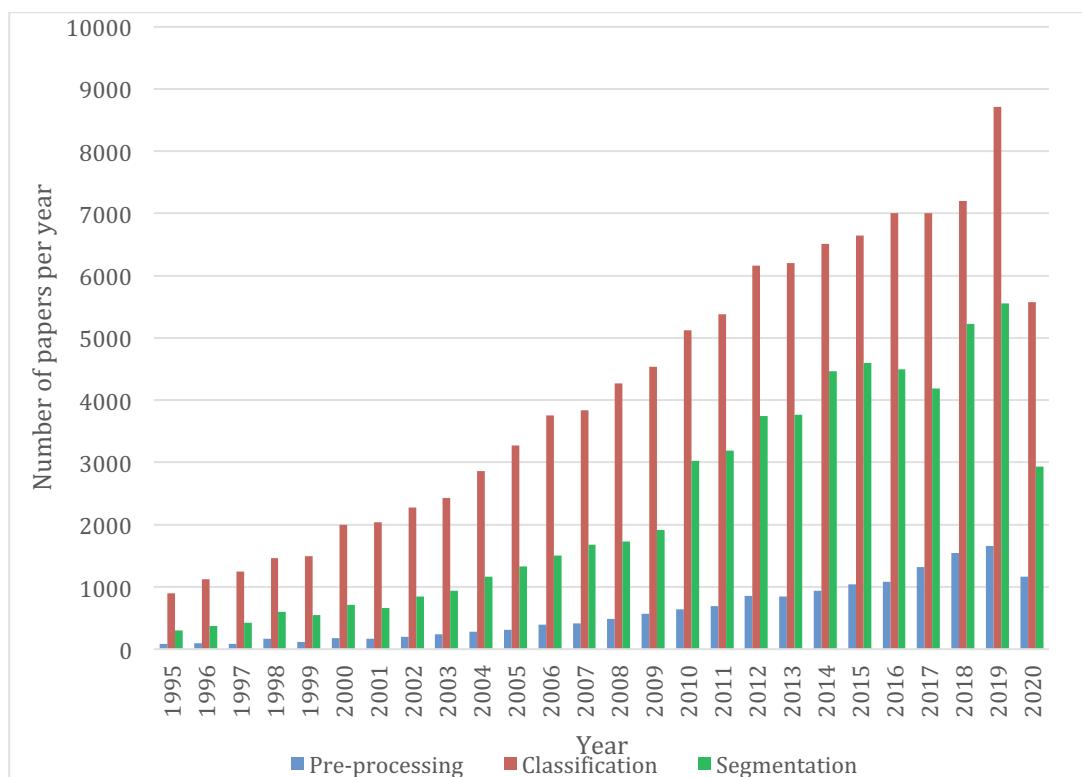


Fig. (4). The graph demonstrates the publication of papers each year on mammogram preprocessing, classification, and segmentation using image processing and deep learning methods for the period 1995-2020. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

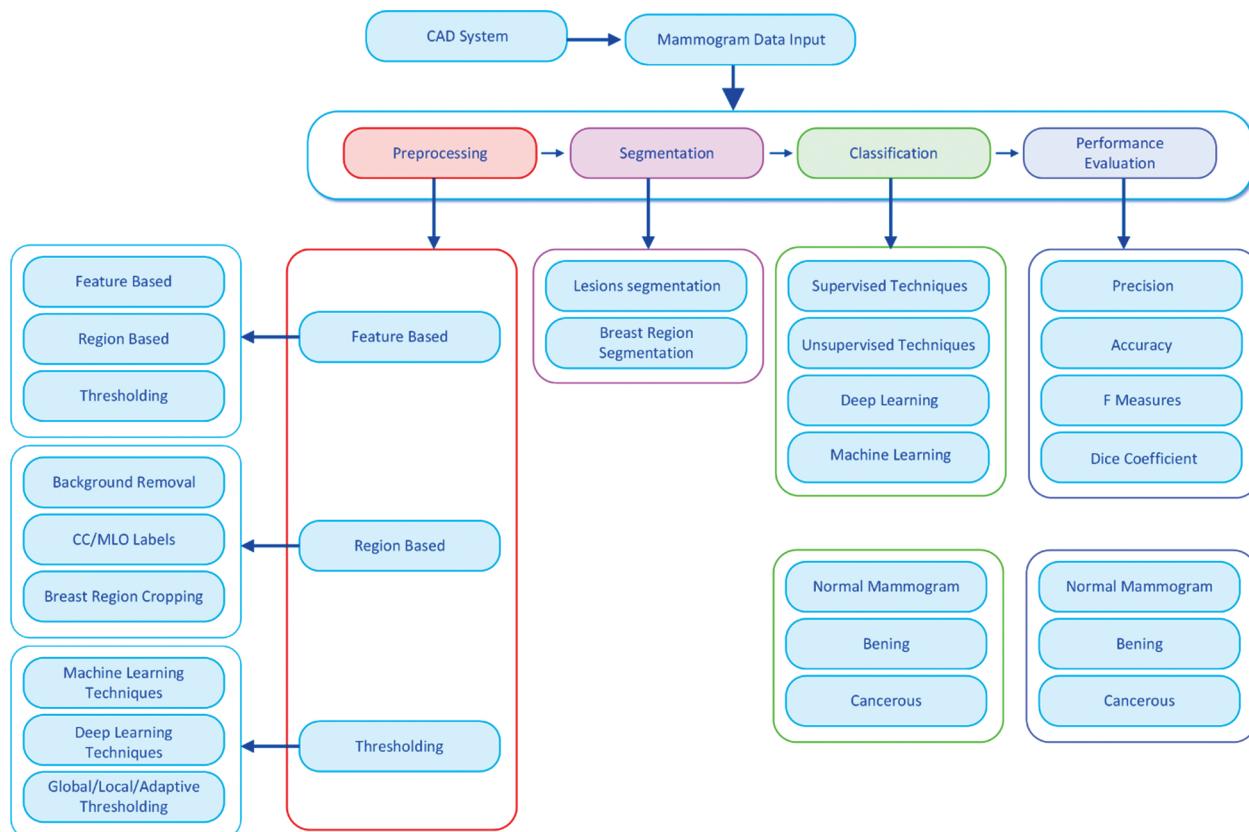


Fig. (5). CAD system pipeline and techniques used at each stage. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

segmentation using image processing techniques and deep learning methods for the period from the year 1995-2020. The first public data available for a mammogram was released in 1994, for this reason, we selected papers from the year 1995-2020. The number of papers for mammogram preprocessing is consistent as the publicly available datasets for mammograms contain low-resolution issues, artifacts present in the mammogram, variant size of mammogram image, pectoral muscle, and labels. A large number of papers are available for mammogram classification tasks including mammogram classification into normal *vs.* benign, mass *vs.* calcification, and benign *vs.* malignant. In addition, many authors used either a single view or both views (taken at 45 and 90 degrees) of the same breast, while other authors used both left and right breast mammograms for classification. The researcher's main focus was on mammogram overall classification; therefore, we have a large number of papers available for classification. Mammogram segmentation is one of the most important steps for a complete automated system to help the radiologist in finding cancer location, size, and possible treatments. Therefore, this survey is mainly focused on mass and microcalcification segmentation using machine and deep learning techniques.

3. THE PIPELINE OF CAD SYSTEMS

In this section, we discuss different steps involved in a CAD system for mammograms as outlined in Fig. (5) and briefly discussed as follows:

3.1. Dataset

The performance of automated CAD models depends on datasets. However, a large amount of data is required for deep models as compared to traditional machine learning models. Unfortunately, in the medical field, detailed annotated data are not available. A mammographic database usually contains mass area, calcification, and architectural distortion. Only few openly free datasets are available for mammograms including i) Digital Database for Screening Mammography (DDSM) [14], ii) INbreast dataset [15], iii) Mammographic Image Analysis Society (MIAS) database [16], iv) Breast Cancer Digital Repository (BCDR) [17], v) BancoWeb [18], vi) Curated Breast Imaging Subset of DDSM (CBIS-DDSM) [19]. One patient sample is shown in Fig. (6) taken from DDSM. Tables 3 and 4 present the dataset privately (paid) and publicly (free) available for a mammogram, respectively [20-24].

3.2. Image Preprocessing on Mammograms

Mammogram preprocessing plays a significant role in achieving ideal results at different stages of a CAD system such as segmentation and classification tasks. In mammographic screening and diagnosis, two main views are widely used such as the craniocaudal (CC) view (top to bottom view of the breast) and the Mediolateral Oblique (MLO) view (side view of the breast taken at an angle). The preprocessing stage is conducted to remove non-breast regions, delete noise, remove labels present in the mammogram such as CC

Table 2. Survey comparison of this paper with other survey papers.

Year	Focus	Dataset	Mammogram Preprocessing	Lesion Segmentation Using ML and Image Processing	Lesion Segmentation Using Deep Learning	Lesion Segmentation Using Single and Multiple View	Classification of Mammogram	Evaluation Metrics	Challenges and Future Work	Refs.
2020	Mainly focus on deep learning, machine learning, and image processing-based techniques for mass and micro-calcification detection.	✓	✓	✓	✓	✓	✓	✓	✓	Our
2011	This paper aims to examine preprocessing like eliminating the unnecessary noise and unwanted sections approach for mammograms.	-	✓	-	-	-	-	-	-	[8]
2010	Compared the output of seven mass detection methods using a single view of mammograms.	-	-	✓	-	✓	-	-	✓	[9]
2013	This paper reviewed the literature about the use of CAD systems in ultrasound and mammography for breast cancer. Detection and diagnosis.	-	-	✓	-	-	-	✓	✓	[10]
2019	This research intended to survey all current research on deep learning with broad relevance for the treatment of breast cancer. The analysis offered a short description of several well-known deep networks too.	-	✓	-	✓	-	✓	-	✓	[11]
2012	Discussed image processing and basic segmentation techniques.	-	✓	✓	-	-	-	-	-	[12]
2013	This article is an overview of clustering strategies for detecting breast cancer in mammograms.	-	-	✓	-	-	-	-	-	[13]

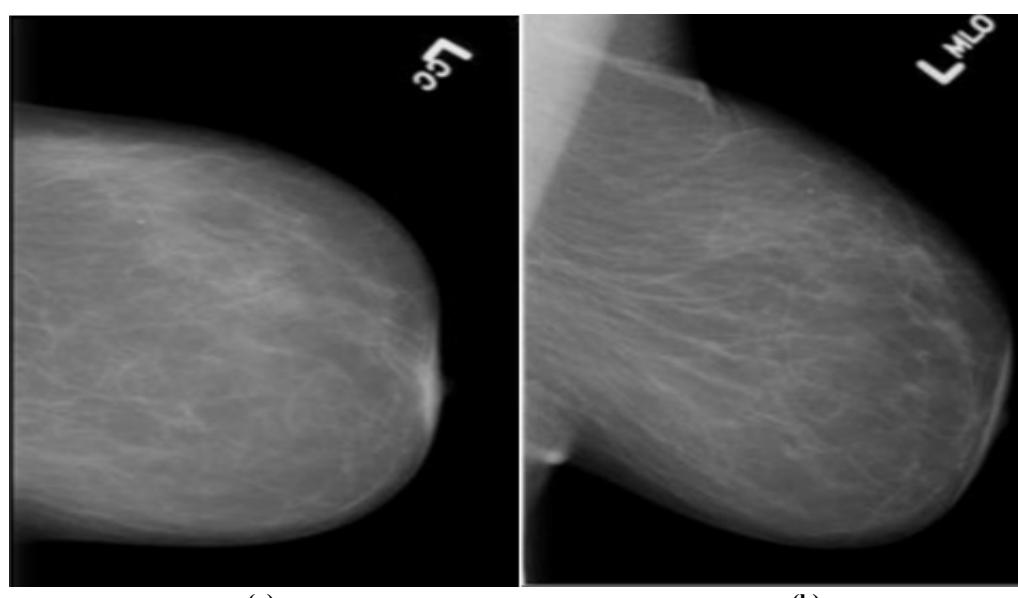
**Fig. (6).** Mammogram of the left breast of the patient with DDSM (a) shows CC view of the left breast, (b) shows MLO view of the left breast. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

Table 3. Paid mammographic database.

Features	Database Names				
	CALMa (Mammo Grid)	LLNL	MIDB	NMDA	OMI-DB
Full form	Computer-Aided Library for Mammography	Lawrence Livermore National Laboratories	Mammographic Image Database	National Digital Medical Archive	OPTIMAM Mammography Image Database
Year	2001	2010	2014	2005	2008
Region	Itlay	USA	The University of California at San Francisco	Universities of Pennsylvania	UK
Number of patient images	3369	198	—	One million	2.000.000
Charges	Only for project members	Paid (100 US\$)	Paid	Paid	Paid
Refs.	[20]	[21]	[22]	[23]	[24]

Table 4. Free mammographic database.

Database Features	Database Names					
	DDSM	MIAS	BancoWeb	CBIS-DDSM	BCDR	INbreast
Strength	Information about different lesion shapes is available. Well-documented and widely used dataset.	Widely used dataset.	Initially designed with a management system that provides the selection options to download required high-quality images.	A Lesion with different shapes and margins is available. This dataset is an updated and standardized version of DDSM.	Standard file format with different resolutions is available along with accurate lesion position.	Accurate and consistent contours are also given in XML format by specialists.
Limitation	The precise position of the lesion is not available. It is not updated anymore.	Small dataset with only MLO view and low-resolution images. Unbalanced combination of malignant and benign findings.	Approximately 32% of the images contain lesion or calcification findings, stored in the archive. 68% of data is still either normal images or images that contain cancer but are still not detected.	Not updated since 2017 and no online support is available.	Limited size.	Lesion mass shape variation is limited.
View	Both MLO and CC	MLO	Both MLO and CC	Both MLO and CC	Both MLO and CC	Both MLO and CC
Image format	LJPEG	Portable Gray Map (PGM)	TIFF	DICOM	TIFF	DICOM
Total number of cases/ Patient	2620	161	320	6775	-	115
Total number of images	10,480	322	1400	10,239	1247	410
Link	http://www.eng.usf.edu/cvprg/Mammography/Database.html	http://peipa.essex.ac.uk/pix/mias/	http://lapimo.sel.eesc.usp.br/bancoweb/	https://wiki.cancerimagingarchive.net/display/Public/CBIS-DDSM#5e40bd1f79d64f04b40cac57ceca9272	https://bcdr.eu/information/downloads	http://medicalresearch.insecperto.pt/breastresearch/index.php/Get_INbreast_Database

(Table 4) contd...

Database Features	Database Names					
	DDSM	MIAS	BancoWeb	CBIS-DDSM	BCDR	INbreast
Available	Free	Free	Free but registration required.	Free	A free subscription is required to access the full dataset.	Permission is required to download the dataset via email. Few datasets are public and some restricted to individual groups.
Origin	USA	UK	Brazil	USA	Portugal	Portugal
Ground Truth	Pixel level ground truth available for the cancerous region	The radius and center of a circle are given around the region of interest (ROI), where cancer present.	ROI available only for a few images	ROI segmentation is available.	lesions outlines are available.	Accurate and consistent contours are also given in XML format by specialists.
Clinical History	Age of patient	Not available	Yes	Age of patient	Yes	Age, family history, and previous biopsies.
Year	1999	1994	2010	2017	2013	2013
Support	NO	NO	YES	NO	NO	NO
Maintenance and upgrade	NO	NO	Yes	NO	Yes	Yes
Breast Image Type	Screen-Film	Screen-Film	Screen-Film and FFDM	Screen-Film	FFDM and related ultrasound images.	FFDM

Table 5. Mammogram Enhancement Techniques.

Enhancement Techniques	Advantages	Disadvantages
Region-based enhancement [37-41]	Suitable for contrast enhancement, mammograms with varying shape and size ROI, without adding noisy artifacts. Best for enhancement of microcalcification in dense breast.	Could not be used for calcification enhancement.
Feature-based enhancement [42-49]	Suited for both masses and calcification enhancement. To retain only higher frequencies, a threshold is used, while other low-frequency values are ignored. Hence, the resulting images include only the high-frequency regions with potential lesions. Therefore, help to segment the cancerous parts in the mammogram.	All results are based on wavelet thresholding value and weight modification functions.
Conventional enhancement [50-55]	Can be used for mammograms' local and global enhancement. Used for mammogram mass enhancement.	Tendency to enhance noise factor in mammograms.
Fuzzy enhancement [56-61]	Useful for boosting the contours of mass and displaying the fine details of mammogram features and suppressing noise using the fuzzy entropy principle. Can be used for both mass and calcification enhancement.	-

and MLO, removal of artifacts, and markers caused by the image acquisition procedure [8, 25-30]. In addition, for the automated CAD system, pectoral muscle removal is an important task as cancer cells and pectoral muscle have the same intensity, which may cause false results [31-36]. Effective elimination of the pectoral muscle is important to prevent erroneous identification; therefore, it reduces time burden and increases precision, aside from reducing inconsistencies in intra-observance. Mammograms are taken from different machines; therefore, size can be varied. For an automated CAD system, resizing all input images are also part of the preprocessing step without affecting the mammogram and cancer size ratio.

Mammogram image enhancement is the process to improve the quality of low contrast mammograms. It helps the CAD system to detect cancer in mammograms and increases the readability of a mammogram. Hence, achieves high diagnostic accuracy. Enhancement techniques can be divided into four categories, namely, region-based, conventional techniques, fuzzy enhancement, and features-based techniques as discussed in Table 5 [37-61]. It is clear from the analysis that results obtained from the fuzzy enhancement strategies are ideally suited for both mass and calcification enhancement.

3.3. Cancer Segmentation

Breast mammogram segmentation is mainly divided into two parts that include i) Segmentation of the breast region from the background and ii) Segmentation of the cancerous part from the breast region. Many authors proposed novel techniques for breast region segmentation [50, 62-66]. However, this paper is mainly focused on the second part. Automatic detection of cancer mammograms is a very critical part and the success of the CAD system mainly depends upon this step. Abnormalities in a mammogram can be categorized into three types that include i) Masses, ii) Microcalcification, and iii) Architectural distortion. Masses can have different shapes (irregular, oval, round, and lobular) and different margins (speculated, obscured, indistinct, and circumscribed) [67]. Calcifications occur as small deposits of calcium that appear on the mammogram as white spots. Furthermore, it can be challenging to assess an architectural distortion because the definite mass could be invisible.

Breasts can be classified into normal or abnormal breasts. Abnormal breasts can be further divided into masses or calcifications. A mass screened on a mammogram can be classified as benign or malignant that is based on its size, shape, nature, etc. Benign tumors have circular or oval shapes and malignant tumors have irregular shapes. Fibroadenomas, cysts, and breast hematomas are benign or noncancerous while, a malignant, abnormal, or cancerous breast tumor is breast tissue that grows abnormally and uncontrollably. On the other hand, calcification can be further divided into micro-calcifications and macro calcification.

Most of the CAD systems can either detect cancer on a multi-view of a mammogram or a single view of a mammogram. In multi-view there are three different scenarios that include i) Mammogram MLO view taken at 45° angle and CC view taken at 90° angle [68-71], ii) Mammogram of the same breast taken at different time slot [68, 72-74], iii) Right and left mammogram of the patient [64, 66, 75-77]. While,

in a single view, only one mammogram is considered as input of the CAD system. Segmentation techniques are mainly categorized into two types that include cancer segmentation using conventional image processing and machine learning and cancer segmentation using deep learning.

3.3.1. Cancer Segmentation Using Conventional Image Processing and Machine Learning Approaches

In literature, many authors proposed different segmentation techniques. Many CAD systems have been proposed for the detection and classification of masses in digital mammograms. The methods used for these CAD systems are divided into two, first is made up of several phases such as preprocessing, segmentation, extraction of feature information, and classification measures, which are focused solely on image processing and conventional machine learning. Second, on the other hand, Convolutional Neural Network (CNN) based techniques are used to automatically learn and extract features in a mammogram for classification tasks, some of these techniques are shown in Fig. (7). We briefly discussed these techniques along with their advantages and disadvantages as follows and a summary of ML and image processing techniques for cancer segmentation in mammograms is shown in Table 6.

3.3.1.1. Thresholding

A widely used thresholding technique for image segmentation is Global Thresholding (GT), mainly focused on global information such as histograms of breast mammograms [78]. It is easy to implement and mostly used for mammogram preprocessing and the output of the GT method is mainly used as input for the next step of segmentation. Mammograms are 2D projections of a 3D breast, therefore GT method cannot identify the region of interest. In addition, false negatives and false positives are too high for the GT methods. On the other hand, Local Thresholding (LT) performs better for mass detection in mammograms, as for every pixel the thresholding value is set locally based upon the intensity values of the neighboring pixels. It only works well if the images contain sharp edges. The computational cost for thresholding methods is very low. Authors in [79] used local adaptive thresholding for segmenting mammographic images that belong to the same class and then adaptive clustering for result improvement. Similarly, in [80] authors used adaptive gray-level thresholding for an initial segmentation of suspicious regions of mammograms, accompanied by the Markov method of the multi-resolution random field.

3.3.1.2. Edge Detection

Edge detection is a conventional method for the detection of abnormalities in a mammogram. It can be suitable for points with rapid changes in gray-level intensity values. It is a human-like approach to obtain disproportionate areas. Highly appropriate for detection of the suspected region of interest, contours, and object boundaries with the lowest noise. However, this approach requires previous knowledge about objects. Moreover, it is not suitable if images containing a very less or high number of edges. Related literature contains flowing edge detector techniques such as Gaussian filter, Sobel filter, watershed Density-weighted contrast enhancement (DWCE), deformable model, logic filters, and Iris filter.

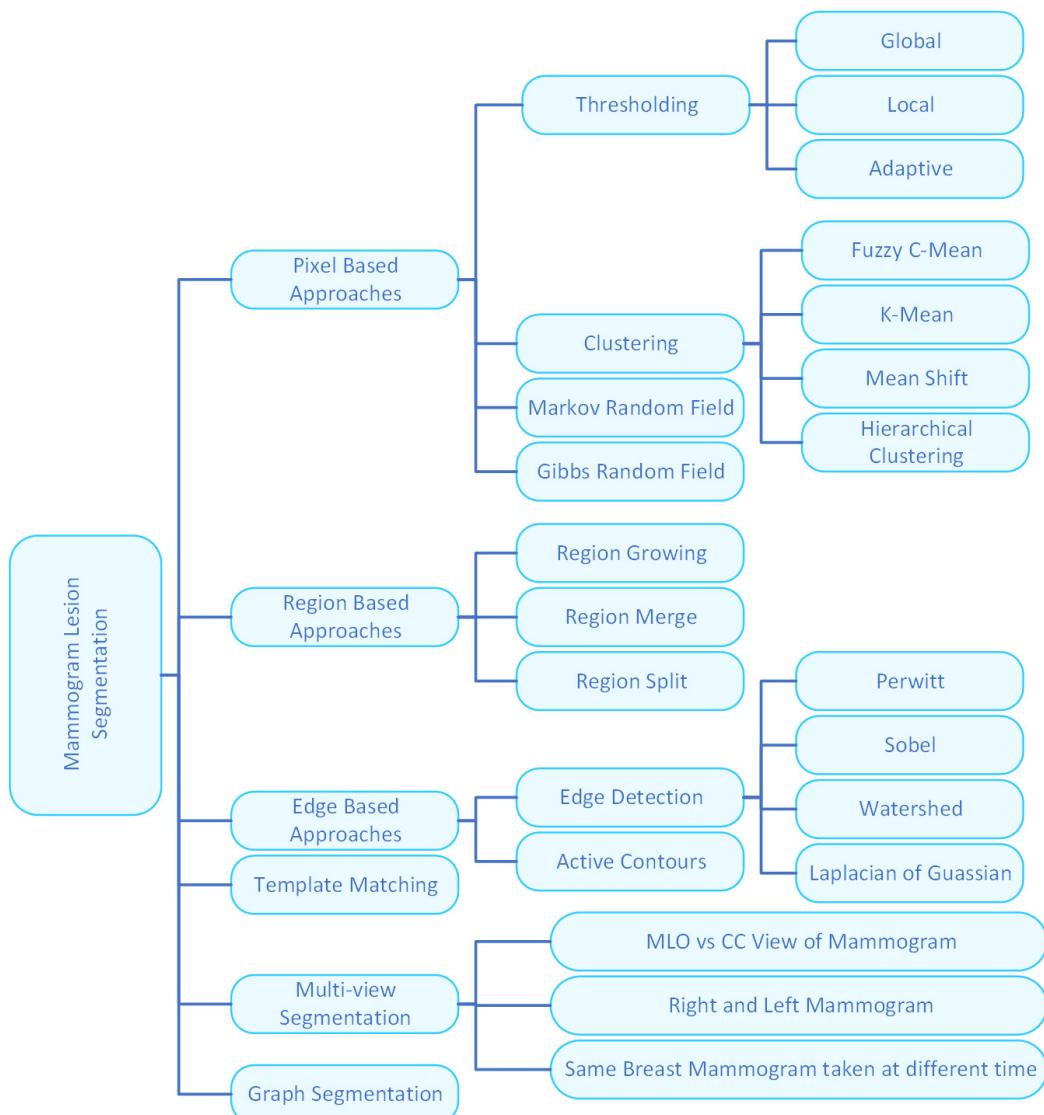


Fig. (7). Lesion segmentation techniques in mammograms.

Zhang *et al.* (2010) proposed an edge-based segmentation model for the identification of mass boundaries in mammograms [81]. At first, contrast stretching and filtering functions are used to remove noise and adjust the contrast of a mammogram. Next, an energy descriptor is computed for each pixel of ROI and finally, the mass region is detected using closed path edges. Abbas *et al.* (2013) proposed a multi-scale framework for mass segmentation using a hybrid of region-based and edge-based algorithms [82]. This hybrid algorithm detects masses accurately irrespective of dense breast, non-smooth borders, and size of cancer.

3.3.1.3. Region-Based

One of the most popular algorithms to segment mass in digitized mammograms is the growing region. The basic concept of this algorithm is to first find a collection of seed pixels in an image, then iteratively expand and aggregate pixels that have similar properties. It uses the properties of pixel communication to expand iteratively and summarize

the area with related pixel properties. The biggest obstacle to the rising area is seeking the correct seeds. It needs an initialization stage, however, a seed point to start with and is highly dependent on the initial guess.

Region clustering searches directly for the regions without prior information. Clustering regions and growing regions are very similar. Examples include the K-means and other adaptive clustering algorithms that are used to segment the volumes. No seed point is needed to initialize; it may search cluster regions directly. Still, the total number of clusters at the initial stage must be predefined. Lee *et al.* (2000) proposed a technique for detecting subtle mass lesions with different ranges of contrast [83]. First, their strategy splits a breast into three regions that include the fatty, dense, and glandular area of a breast. Next, seed collection and segmentation processes are performed with specific threshold values being added to each breast area. Finally, potential masses are categorized using four features representing segmented regions, shape, density, and margins.

3.3.1.4. Pixel Based

There are different types of pixel-based segmentation algorithms that includes Gibbs Random Field (GRF), Markov Random Field (MRF), and clustering. Both the GRF [84-86] and the MRF [80, 87] are powerful modeling tools. To represent the global relationship between pixels, these models used local neighbor pixels. Although the GRF/MRF algorithms provide good results in segmentation. They are, however, computationally costly and time-consuming. Bharadwaj *et al.* (2015) proposed a novel technique to segment micro-calcification in mammograms [84]. At first, a breast region is segmented from the whole mammogram using fuzzy C means clustering. Then top-hat and watershed transformation is used to segment ROI from the breast region. Finally, GRFs are used to analyze the clique patterns on pixel conjunction to detect micro-calcification in the mammogram.

3.3.1.5. Fuzzy Based

Fuzzy techniques are widely used for mammogram lesion segmentation. Since mammographic images often have ambiguous borders and poor contrast strength, the fuzzy set theory is highly effective in analysis of such pictures. There are two main reasons why fuzzy image processing is important. Firstly, as a series of fuzzy if-then rules, fuzzy set theory and fuzzy logic are powerful tools for representing and processing human knowledge. Secondly, image processing contains data randomness, uncertainty, and vagueness; though, fuzzy methods may easily handle these. A variety of advancements have been produced over the last decade in fuzzy image segmentation techniques; still, there is a space for improvement.

3.3.1.6. Others

Bilateral Subtraction (BS) of images is also used to identify suspicious areas. Moreover, known as an asymmetry solution, since it is centered on the natural similarity between right and left breasts. Subtraction of bilateral images is easy to implement. However, it cannot classify true positive regions into benign and malignant masses, since it is difficult to properly differentiate between right and left breasts. In addition, false positives are very high in BS.

Stochastic Relaxation (SR) is an unsupervised form of segmentation with evidently limited optimization aimed at identifying all different lesions. In a statistical model, it is often used by constructing an optimal label map to separate cancerous tissue from normal regions. It is computationally intensive, time-consuming, and requires the estimation of complex parameters.

Multi-Scale techniques (MS) can transform the mammogram images from the spatial domain into the frequency domain before segmentation of an image using Discrete Wavelet Transform (DWT) filters. It increases the detection rate if the suspect regions are identified correctly. The main drawback of this technique is the selection of proper initial wavelet and weight modification functions. Authors of [88] proposed multi-scale algorithms to enhance raw full-field digital mammograms by identifying suspicious masses using a two-stage segmentation process. Furthermore, they extracted the texture features of morphological and spatial gray-level de-

pendedence for each suspicious mass. Finally, stepwise linear discriminant analysis with simplex optimization is used to select the most useful features, which were used to differentiate normal from mass tissues. Similarly, the study [89] proposed a model based on a single view for lesion detection and a classifier for correspondence. The output of the classifier is used for biasing the selection of training patterns for the CAD multi-view system.

Template Matching (TM) is the most employed method for the segmentation of medical images. By comparing samples, it incorporates previous knowledge of mammograms and segments possible masses from the background. It is easy to implement and produce good results if prototype/ground truths are selected appropriately. However, it requires prior information regarding the region's properties like shape, surface area, and size. TM models may result in many false positives. Lochanambal *et al.* (2010) proposed TM based novel model for cancer segmentation in mammograms [90]. Based on the shape, size, and brightness of microcalcifications and masses, templates are defined. Before TM, mammograms, images are enhanced using median filters and an edge detection operator. Similarly, the study [91] proposed a hybrid technique to segment breast masses on mammograms based on dynamic programming and TM.

3.3.2. Cancer Segmentation Using Deep Learning

Precise mass segmentation is the key to increasing the accuracy of breast cancer screening and lowering mortality rates. Reviewing a film is time-consuming for a specialist. Moreover, conventional medical segmentation techniques frequently involve advanced expertise or manual feature extraction, frequently leading to a subjective diagnosis. In traditional methods of segmentation, some parameters (such as thresholds) must be set and effective features extracted manually, which could be based on experience. The results of such techniques are therefore not just consistent. Furthermore, despite the nature of noise and mammographic artifacts, the background area is complex, and the mass size is too small compared to the background region. Also, the effect of conventional approaches to segmentation is not optimal. These conventional methods have difficulties in automatically achieving accurate end-to-end segmentation of the breast mass (Table 6) [92-101].

Recently, Convolutional Neural Network CNNs, and deep learning show exceptional visual recognition performance. CNN's representational learning ability has also been applied effectively to medical image processing and mammography recognition. Le *et al.* (2019) proposed Multi-Task Learning (MTL) scheme that combines segmentation at the pixel level with classification annotation at the global image level [102]. A fully Convolutional Network (FCN) based model is used to extract local features with the Residual neural network (ResNet). Classification and segmentation performances are 38.28 and 84.02 for Mean Dice and Area Under Curve, respectively.

Min *et al.* [103] suggested a CAD system for cancer segmentation that involves only pseudo-color image generation along with Mask R-CNN. First, object-like patterns in a mammogram are amplified using multi-scale morphological sifting and convert these grayscale images into pseudo color.

Table 6. Summary of Machine Learning and image processing techniques for cancer segmentation in mammograms.

Technique	Method Explanation	Mass Type	Performance Evaluation (Sensitivity/Accuracy)	Refs.
Pixel	Mammogram images were divided into multi-resolution representations, then for each part at every pixel four features were extracted, and a binary tree classifier is used for mass detection.	Detect speculated cancer of different sizes.	84.2%	[92]
	A hybrid model for mass detection, which combines discrete wavelet transform, a dogs-rabbits algorithm with fractal dimension analysis.	Detect ill-defined masses, boundaries, circumscribe, and speculated mass types.	97.3%	[93]
	Used SVM for mass shape classification and to decrease false positives. Multiresolution is used for images having redundant information.	Detect architectural distortions, masses of different shapes like speculated, oval, and circumscribed.	80%	[94]
	Proposed a model-based active contour algorithm, termed "snakules". In addition, a radial speculation filter is used for spatial location detection.	Detect Speculated masses.	86%	[95]
	The median filter is used for noise smoothing. To detect masses, a thresholding-based technique is used. Mainly focused on the location of cancer rather than shape.	All types of masses.	95.91%	[53]
	K-mean clustering is used for image segmentation. To describe the texture of the segmented region cooccurrences matrix is used. Finally, to classify mass, vs non-masses shape, and texture features used with SVM.	Benign vs malignant mass.	85% accuracy	[96]
Fuzzy Based	For image enhancement and feature extraction, a wavelet transformation function is used; the classification process uses a combination of algorithms of an adaptive neuro-fuzzy inference system.	Mass vs calcification, and benign vs. malignant mass.	Benign vs malignant Accuracy = 93.7% Mass vs. microcalcification = 87.5%	[97]
	A hybrid approach is used that consists of fuzzy image enhancement sets and rough sets for producing minimum attributes and rules that are used as a classifier for the various regions of interest.	All mass segmentation.	Accuracy = 98%	[98]
	lazy snapping algorithm was used with K-mean and fuzzy c-mean methods for mass boundaries detection.	Accurately detect boundaries of all types of masses.	94.12% accuracy	[99]
	A novel approach to designing weighted Fuzzy rules interpolation CADx systems for mass mammographic image classification.	Benign vs malignant mass.	91.65% accuracy	[100]
	Segmentation approaches are formulated based on fuzzy morphology and classical morphology. By comparing the results of both techniques conclusion is that the identification of tumor boundaries with fuzzy morphology provides higher accuracy than the findings in classical morphology.	Speculated masses.	60.69%	[101]

Transfer learning is adopted with the Mask R-CNN to identify and segment masses on the pseudo-color images simultaneously. The process, tested on the INbreast public dataset, outperforms state-of-the-art methods by obtaining an average true positive rate of 0.90 and 0.88 dice score for segmentation.

The study (67) proposed a conditional Generative Adversarial Network (cGAN) based model for cancer segmentation from the ROI of a mammogram. The Generators draw a binary mask to learn about tumor areas and the adversarial

network distinguished between real and generated masks. The proposed model achieved 87% Intersection over Union (IoU) and 94% Dice coefficient on INbreast and private datasets. After cancer segmentation, the author proposed CNN based shape descriptor. That further classified cancer into four shapes such as round, oval, lobular, and irregular. The DDSM dataset is used for the shape classification task, as this publicly available dataset can provide information about cancer shapes. The overall accuracy of the system is 80%. A summary of deep models for cancer segmentation from mammograms is presented in Table 7 [103-107].

Table 7. Deep learning techniques for lesion segmentation in mammograms.

Technique	Method Explanation	Mass Type	Performance Evaluation (Sensitivity/Accuracy)	Validation Approach	Refs.
Mask R-CNN	The first object-like patterns in a mammogram are amplified using multi-scale morphological shifting and convert these grayscale images into pseudo-color. Transfer learning is adopted with the Mask R-CNN to identify and segment masses on the pseudo-color images simultaneously.	All masses (benign and malignant)	0.88% dice score	Train/test split	[103]
MNPNet	Proposed novel multi-level nested pyramid model to resolve interclass indistinction and intraclass variation through capturing contextual information in the mammogram.	All masses	Dice Score for INbreast is 91.10% and for DDSM-BCRP, 91.69%	Train/test split	[104]
AG-UNet	Proposed a fully automated system for breast mass segmentation based on deep learning, integrating a densely linked U-Net with attention gates (AGs). The encoder is a densely connected and the decoder is an optimized U-Net decoder with AGs.	Benign and malignant masses with Oval, round and irregular outlines.	DDSM was used for testing and training. F1-Score: 82.24% AUC: 0.8605 Sensitivity: 77.89%	Train/test split	[105]
PNF + Faster R-CNN	The proposed novel method focused on deep learning to identify both calcification and masses in mammograms. Their process blends Faster R-CNN to achieve the maximum efficiency in mass detection with Pyramid Network Feature (PNF), Non-Local Neural Networks, and Focal Loss.	Segment both masses and calcification.	Training to localize the masses dataset used: INbreast, BCD, and CBIS-DDSM. For training of calcification and testing both masses along with calcification, the author used a private dataset. Average precision: 0.933% Recall: 0.976%.	Train/test split	[106]
AUNet	Suggest a novel asymmetrical encoder-decoder structure along with an attention-guided dense-upsampling network (AUNet) for specific breast mass segmentation directly into entire mammograms.	Masses	Dice similarity coefficient of CBIS-DDSM: 81.8%, INbreast: 79.1%	K-Fold cross-validation.	[107]

3.4. Mammogram Classification

The final step for automated CAD systems is to classify input images into normal or cancerous. Cancerous images can be further classified into masses or calcification. Masses and calcification can be classified into benign or malignant based on their shape, size, and nature. In the literature, a lot of work has been done on mammogram classification steps. Some authors apply segmentation steps after classification. Deep models like VGG with different layers like 9, 11, 16 and 19 [108-110], GoogleNet [111-114], ResNet [115-117], are used for mammogram classification.

More data are required for the classification task using deep learning. Also training the generator in GANs required a large amount of data. Therefore, researchers used different augmentation techniques. To increase data size, many au-

thors used GANs to artificially generate the dataset. Many researchers used a single view of mammograms [117-121] for classification. To increase information, recently, the authors used multi-view of mammograms as input, so maximum information can be given to the model and achieve high performance than a single mammogram [122].

Transfer learning is another technique used for mammogram classification [112, 123-126]. Two strategies are used for transfer learning, pre-trained model with ImageNet dataset and fine-tune the model on a mammogram. While on the other hand, researchers used VGG and other standard classification models for classification and trained these models from scratch. However, the number of parameters is too high. To handle this issue, the authors used a MobileNet-based model for transfer learning, which achieves high accuracy

Table 8. Mammogram classification model.

Classification	Dataset	Accuracy	Mammogram View	Input	Technique	Refs.
Binary	INbreast	85.86%	Single	Whole Mammogram	Otsu's Segmentation + AlexNet	[128]
Three-class (normal, benign, and malignant)	IRMA	83.74%	Single	Mammogram Patches	CNN-discrete wavelet + CNN-curvelet transform	[129]
Normal and abnormal	MIAS	96.97%	Single	ROI's	Discrete Wavelet Transform + Support Vector Machine	[130]
Benign or malignant images	MIAS	93%	Single		Wavelet Features	[131]
Cancer or no-cancer	DDSM	ROC: 0.92	Single	Whole Mammogram	ResNet	[132]
Multi-class (Cancerous or normal, Further, classify cancerous into benign and malignant)	DDSM	86.8%	Single	Whole Mammogram	Transfer Learning + MobileNet	[127]
Binary (Malignant vs. normal)	DDSM	AUC: 0.896	Single	Mammogram Patches	GAN + ResNet-50	[133]
Multi class (mass vs. calcification and malignant vs benign)	CBIS-DDSM and mini-MIAS	93.73%	Multi-views	Mammogram Patches	Transfer Learning + VGG-16	[122]
Three-class (Normal, benign and malignant)	DDSM and IN-breast	AUC: 0.86	Multi-Views	Whole Mammogram	Transfer Learning + AlexNet	[134]
Binary (Benign vs. malignant)	BCDR	0.85%	Multi-Views	ROI's	RNN + Attention Mechanism	[135]

with a smaller number of parameters [127]. Table 8 shows the techniques used for mammogram classification [128-135].

3.5. Evaluation of CAD Systems

In this section, we discussed different evaluation measures to evaluate the performance of CAD systems for mammograms. Either classification of mammograms or segmentation of lesions within the mammogram is the final step for CAD systems. A confusion matrix is a table that is used to assess a classification model's performance, as shown in Table 9. In case of classification, TP (systems predict mammograms as cancerous when they are actually cancerous), FP (systems predict mammograms as cancerous when they are actually non-cancerous), FN (systems predict mammograms as non-cancerous when they are cancerous), and TN (system predict mammogram as non-cancerous when they are non-cancerous). On the other hand, for the segmentation task, TP (correctly segmented lesion within the ROI), FP (segmented lesion outside the ROI), FN (not segment full lesion within the ROI), and Ground Truth (GT) are the actual boundary of the lesion within a mammogram identified by

expert radiologists. First, TP, FP, TN, and FN are calculated. Then, these are used to calculate other performance measures used for the classification or segmentation tasks as shown in Table 10.

4. CRITICAL DISCUSSION AND FUTURE GUIDELINES

A lot of research has been performed on the treatment of breast cancer. This conducted survey presents image processing techniques and deep learning techniques used in different stages for a fully automated CAD system for mammograms. The review indicates that DL models have helped to enhance the CAD systems for breast cancer diagnosis efficiently, still, difficulties remain for these approaches to be clinically effective and further improvements are required. From the survey, we noticed a few challenges for mammograms and presented possible solutions for these challenges.

The success of any deep learning model is based on the size of the dataset used for training and testing. Unfortunately, for mammograms, few public datasets are available. These datasets are now old in technology and any CAD system

Table 9. Confusion Matrix used for the binary classification task.

Predicted	Actual	
	Positive (cancerous)	Negative (Non-cancerous)
Positive (cancerous)	True Positive (TP)	False Positive (FP)
Negative (Non-cancerous)	False Negative (FN)	True Negative (TN)

Note: Def stands for definition.

Table 10. Evaluation measures.

Term	Formula	Definition
Accuracy	$\frac{TP + TN}{TP + FP + TN + FN}$	Accuracy is the percentage of an overall number of accurate observations.
Specificity	$\frac{TN}{TN + FP}$	The total number of negatives that were correctly identified as negative. Often called True Negative Rate (TNR).
Sensitivity	$\frac{TP}{TP + FN}$	Often called True Positive Rate (TPR) or Recall.
The area under the curve (AUC)	$(Sensitivity + Specificity) * \frac{1}{2}$	AUC meaning indicates the capacity of the classifier to prevent the misclassification.
F1 score	$\frac{(Recall * Precision) * 2}{Recall + Precision}$	A balancing metric is used to see a trade-off between recall and precision. Moreover, known as the dice coefficient.
Precision	$\frac{TP}{TP + FP}$	The ratio between the true positive and total number of predicted positive classification.
Receiver Operating Characteristic (ROC) curve	-	ROC curve maps FPR and TPR, respectively, on the x-axis and y-axis. The smaller FPR value means a better classifier. Bigger TNR and TPR values mean a better classifier.

trained on these datasets may not accurately work in a clinic's mammogram acquired from the latest machines due to changes in size and resolution of input images *etc.* Apart from the dataset size issue, large computational power, data preprocessing, and extensive experiments are required for DL models which make them difficult to be used in a real-time scenario. To resolve this issue, research partnerships, as well as specific channels for data exchange, should be supported by numerous research centers. In addition, organizing competitions among researchers is a way to get the best model which can be used in clinics and hospitals to serve humanity.

Most of the models available in the literature require ground truth (annotated data) at pixel level or image level. An expert radiologist is required for data annotation, which is a time-consuming, expensive task and experts are rarely available. *Inter* and *intra*-variance are also present in annotated data, which is the most difficult task to annotate data 100% accurately. Hybrids of supervised and unsupervised techniques can be used to resolve this issue. Since few datasets are publicly available regarding mammograms; therefore, very limited work has been done for mammogram preprocessing. Basic filters and traditional image processing techniques are used for noise, artifacts, pectoral muscle, and extra region removal. There are still some gaps for deep learning-based techniques to automatically remove the pectoral muscles and increase the resolution of the mammogram.

Women with higher density may have higher chances of developing cancer. It is still a very challenging task to detect

cancer in mammograms of the dense breast due to more connective tissue of fibro glandular tissues than fatty tissue. It is very hard to find cancer within dense mammograms since cancers and dense tissues look white in mammograms. Currently, in clinical practices, a radiologist visually assesses mammograms for calculating breast density scores using the Breast Imaging and Reporting Data System (BI-RADS). BI-RADS I, II, III, and IV are used for entirely fatty, scattered, fibro-glandular, heterogeneously dense, and extremely dense, respectively. A possible solution to localize cancer in a dense mammogram is 2D to 3D generation. Up till now, no research is available for mammogram 3D generation from 2D. A lot of work can be done in this direction. In the medical field, it would help to reduce the chances of death. We can prevent 7 lives from 1000 women who have BC. Moreover, it would reduce the risk of having to undergo chemotherapy at an early stage of cancer. Machine learning and deep learning play a vital role to decrease the mortality rate and increase the accuracy as shown in Tables 6 and 7.

Models available for lesion segmentation can only localize mass or calcification at a time. A single mammogram may contain both mass and calcification. In addition, no such research is available to handle a single mammogram containing multiple masses. Apart from cancer localization, there is still further classification of cancer into shapes (Oval, round, *etc.*) and based on this to suggest further treatment options like a biopsy, *etc.*

To handle the overfitting issue in deep models due to the small size of the dataset, many researchers performed basic

data augmentation like rotation, zooming, cropping, etc. However, these techniques are not able to overcome the class imbalance issues. In addition, the reduction of false positives and false negatives may not be resolved by these traditional techniques. GANs-based models and transfer learning-based techniques can be used as a possible solution for this issue. The data size issue is not only for the mammogram data but also an issue for other medical images. Up till now, no model is available for medical images which can be used for transfer learning and researchers have used ImageNet for transfer learning. In the future, a large model could be developed which could be fully trained on medical images and that model can be specifically used for a mammogram and other medical images.

CONCLUSION

Our systematic review explored an extensive study of state-of-the-art image processing, ML, and DL-based segmentation techniques to provide an in-depth review in this field to non-experts and beginners. Our goal is to address the intrinsic challenges that could occur in the segmentation of cancer in mammograms which helps to improve a fully automated CAD system. It could help to develop a secure and computationally effective CAD method to support clinicians in early-stage breast cancer diagnosis. The segmentation of cancer in mammograms is an important final step and further cancer treatment, such as biopsy, depends entirely upon it. Analysis of mammograms helps to reduce the high number of false positives and false negatives to get rid of useless biopsies.

Heterogeneous densities and lack of publicly available datasets of a breast, make masses more difficult to detect and classify. The conventional ML methods provide restricted approaches that are constrained to either specific types of density or particular datasets. DL methods show significant progress in the diagnosis of breast cancer. We have also investigated the issues of data deficiency and computational cost of DL models; however, these issues have been largely solved by implementing different augmentation techniques as discussed earlier in this review. Moreover, we have identified several issues that are present in conventional ML and DL techniques along with their possible solutions.

AUTHORS' CONTRIBUTIONS

WA drafted the first write-up of the paper and carried out the literature review the major contribution to this study. BR analyzed and reviewed the paper. supervised this work in designing the structure of the paper and reviewed the paper. All authors read and approved the final manuscript.

LIST OF ABBREVIATIONS

BC	= Breast Cancer
BI-RADS	= Breast Imaging and Reporting Data System
BS	= Bilateral Subtraction
CAD	= Computer-Aided Diagnosis
CC	= Craniocaudal
CNN	= Convolutional Neural Network

DL	= Deep Learning
DWCE	= Density Weighted Contrast Enhancement
DWT	= Discrete Wavelet Transform
FCN	= Fully Convolutional Networks
GAN	= Generative Adversarial Network
GRF	= Gibbs Random Field
GT	= Global Thresholding
LT	= Local Thresholding
ML	= Machine Learning
ML	= Machine Learning
MLO	= Mediolateral Oblique
MRF	= Markov Random Field
MTL	= Multitask Learning
ResNet	= Residual Neural Network
ROI	= Region of Interest
SR	= Stochastic Relaxation
TM	= Template Matching
TNR	= True Negative Rate
TPR	= True Positive Rate
WHO	= World Health Organization

CONSENT FOR PUBLICATION

Not applicable

STANDARDS OF REPORTING

PRISMA guidelines and methodology were followed.

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CONFLICT OF INTEREST

The author(s) declare no conflict of interest, financial or otherwise.

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SUPPLEMENTARY MATERIAL

PRISMA checklist is available as supplementary material on the publisher's website along with the published article.

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