Volume: 13 Issue: 06 Pages: 5197-5214(2022) ISSN: 0975-0290

Deep Learning Techniques for Improving Breast Cancer Detection and Diagnosis

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ABSTRACT

In this paper, we aim to introduce a survey on the applications of deep learning for breast cancer detection and diagnosis to provide an overview of the progress in this field. In the survey, we firstly provide an overview on deep learning and the popular architectures used for breast cancer detection and diagnosis. Especially we present four popular deep learning architectures, including convolutional neural networks, fully convolutional networks, auto encoders, and deep belief networks in the survey. Secondly, we provide a survey on the studies exploiting deep learning for breast cancer detection and diagnosis.

Keywords**: Deep Learning (DL), Breast Cancer, breast cancer detection**.

Date of Submission: May 10, 2022 Date of Acceptance: Jun 04, 2022

I. 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 2022 report, more than 1.7 million women in 2022 were diagnosed with breast cancer world-wide. This is considered around 11.9% of all cancers diagnosed in the same year with 522000 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 effort s 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 reduce 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 dig- ital mammography (FFDM) augmented with CAD tools. The study showed that CAD combined with mammography presented 100% sensitivity in identifying cancers manifesting as micro-calcifications 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].

There have been numerous studies in the literature investigating the use of CAD systems for breast cancer detection and diagnosis. These studies have used various imaging modalities and machine learning algorithms, some of which have even gone through clinical workflow for feasibility tests [14, 15]. However, the success of these

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studies has been limited due to high phenotypic variations in tumors, large number of false positives, and poor diagnosis rates [16]. For these reasons, many studies were dedicated to improving these systems. Lately, research in this field is moving towards a more favorable direction due to exciting new advances in machine learning, specifically "deep learning" [17, 18].

Deep learning, i.e. as deep neural networks, has been a rapidly growing subfield of machine learning. The main reasons behind this breakthrough over the past few years are increased availability of more advanced computer algorithms that are inspired by human intelligence, updates on contemporary hardware technology for processing and storing large data sets, and an increased availability of massive amounts of labeled data to train these algorithms with better precision. This revolutionary and cutting-edge approach to computer vision has had a broad spectrum of applications including graphics, genetics, medicine, the automotive industry, the Internet, and ultimately, radiology and imaging sciences [19-23].

In AI technology, deep learning methods have multiple levels of representation learning which use raw data and discover the essential representations for detection or classification [24]. These inherent representations and patterns are obtained through a hierarchical framework which is able to put features extracted from a low level (starting with raw data) and high level abstracts together using a non-linear approach. Such networks are able to improve themselves according to the input content variation and optimize the relationship between inputs and outputs via an iterative training process [25]. At the same time as the deep learning concepts were developed, a step-change in processing power through high performance GPUs 15 and open source frameworks/libraries developed on CUDA 16 (CUDA (2017)) or OpenCL 17 (OpenCL (2017)) platforms have made significant progress for the implementation of deep learning based methods. These open source frameworks and libraries provide the chance for optimized implementation of convolutions and other related functions. In addition, they facilitate the ability to perform a high number of computations at relatively low costs through their massive parallel architectures.

This paper presents an overview of different deep learning based approaches used for mammography and breast histology and proposes a bridge between these two fields employing deep learning concepts. We have focused on mammography, since this is the most common modality used in breast screening, and H&E stained histology, since it is considered as the gold standard for final decision making.

II. BASIC CONCEPTS OF DEEP LEARNING

Machine learning, or learning that occurs without explicit programming, can take place in one of two forms: conventional, "shallow" learning (neural networks with a single hidden layer or support vector machines), or deep learning (neural networks with many hierarchical layers of nonlinear information processing). Deep learning was recently reviewed in detail by [24] While deep and shallow learning differ in more than one way and both approaches have value in specific applications, the takeaway difference is that shallow learning does not deal well with raw data, requiring extensive human input to set up and maintain, whereas deep learning can be largely unsupervised once set in motion, learning intricate patterns from even high-dimensional raw data with little guidance.[24] Ref. [25] referred to this as optimizing the breadth/depth trade-off; 2 that is, only a deep circuit can perform exponentially complex computational tasks without requiring an infinite number of elements.[25] The importance of this is most readily apparent in the areas where deep learning has been shown to be useful: image and language recognition [26] and video games [27] are two common examples, or, perhaps more interestingly, replication of painting styles or even composition of classical music.[28] The type of learning required in these tasks is representation learning; that is, detecting or classifying patterns, or representations, from raw data,[24] particularly when this data is heirarchical in structure. Image recognition, for example, begins with learning a progressive hierarchy of subimages from pixels, starting with edges, then motifs, until the final output is a whole object.[24] Representations are formed through simple associations using, for example, pixels as raw data, not by human labeling or preprogrammed logic. Being essentially unsupervised algorithms, deep neural networks can act as feature detector units at each layer (level) that gradually extract more sophisticated and invariant features from the original raw input signals. One can imagine the impossible effort of annotating the millions of images that machines can now accurately identify. That machines can now distinguish images of two nearly identical objects or complete a sentence is all possible increasingly with help from deep learning. These and other recent developments in DNN architectures have boosted enthusiasm within the machine learning community, with unprecedented performance in many challenging tasks [29, 30]. They have also raised important questions about whether deep learning could also automate tasks like annotation, image recognition, prediction, and classification in similar biological applications, where the sheer amount and complexity of data has surpassed human analytical capabilities.

I. Why Deep Learning May Benefit Biomedical Research

With some imagination, parallels can be drawn between biological data and the types of data deep learning has shown the most success in, image and voice data. A gene expression profile, for instance, is essentially a "snapshot", or image, of what is going on in a given cell or tissue under given conditions, with patterns of gene expression representative of physical states in a cell or tissue in the same way that patterns of pixelation are representative of objects in a picture. In the same way that two similar but categorically different images must be discerned by deep learning algorithms regardless of background or position, two similar but categorically different disease pathologies may be difficult to distinguish if certain unimportant background conditions happen to match (e.g., tissues, time

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points, individual, species, platform), thus selectivity of key differences is essential. Alternatively, one pathology may appear to differ from itself when imposed on a variety of different experimental "backgrounds" and in several different states of progression, so invariance to non-target-related differences is also key. These features, selectivity and invariance, are requirements for both image recognition and gene expression analysis and are also two hallmarks of CNNs, the powerhouses of modern visual image processing.[24] The same type of analogies can be drawn with other applications of deep learning: language prediction, for example, requires sequential learning with recurrent neural networks[24] and can be paralleled with signaling cascades in biology, where one event can be predicted from previous upstream events in the same way that one word in a sentence can be predicted from the previous set of words. Structural prediction would be another example. The possibilities are endless; with enough interest in the topic, any number of other parallels can be drawn and new applications conceived. These parallels, while illustrative and hypothetical in nature, are also backed up by several practical advantages of DNNs that strengthen the case for biological application. First, DNNs require very large data sets, which biology is teeming with at this time. Second, DNNs are well-equipped to handle high dimensional, sparse, noisy data with nonlinear relationships, all of which are common to transcriptomics and other -omics data in biology. Third, DNNs have high generalization ability; once trained on a data set, they can be applied to other, new data sets; this is a requirement for binding and interpretation of heterogeneous multiplatform data, such as gene expression data.

Finally, these considerations are further supported by the fact that the small numbers of deep learning studies in biomedicine that now exist have shown success with this method. These are to be discussed below. Importantly, despite the suitability of DNN for biological data and the potential applications, the adoption of deep learning methods in biology has been slow. This may have several explanations. While deep architectures can be exponentially more efficient than conventional models, capturing fine subtleties in the structure of the data, [31] DNNs, especially recurrent networks, are very complex machines containing hundreds of millions of weights, which makes training and regularization difficult. Deep models are still not optimized, still lack an adequate formulation, require more research, and rely heavily on computational experimentation. It should also be emphasized that, despite being able to extract latent features from the data, DNNs are black boxes that learn by simple associations and co-occurrences. They lack the transparency and interpretability of other methods and may be unable to uncover complex causal and structural relationships common in biology without some human interpretation. Nevertheless, their many benefits may outweigh these obstacles, some of which may be overcome with time.

II. Deep Learning Methods

The goal of this section is to provide a formal introduction and definition of the deep learning concepts, techniques and architectures that we found in the *breast cancer detection and diagnosis* papers surveyed in this work.

Neural networks

Neural networks are a type of learning algorithm which forms the basis of most deep learning methods. With respect to artificial intelligence, are inspired by the biological basis of neural networks, in which neurons can sense their environment and communicate information to surrounding neurons. In artificial intelligence, neural networks are typically represented by layers. These layers are, essentially, computational functions that process input information, as it compares to training data, to predict an outcome (i.e. f(x) =y, where x is the input information, and y is the outcome prediction). Input neurons can sense new data and pass information onto neurons within different layers, processing this information. Connections between neurons are called "synaptic weights", which are coefficients used to amplify or dampen the input signal by multiplication, assigning significance to the input to obtain the corresponding output.[28] The computational power of these networks relies on the extent of training data that is available, allowing these neural networks to update weights of the connections. Simple network structures with only a few layers are known as "shallow" learning neural networks, whereas network structures which employ numerous and large layers are referred to as "deep" learning neural networks.

Convolutional neural networks (CNNs)

There are two key differences between MLPs and CNNs. First, in CNNs weights in the network are shared in such a way that the network performs convolution operations on images. This way, the model does not need to learn separate detectors for the same object occurring at different positions in an image, making the net- work equivariant with respect to translations of the input. It also drastically reduces the amount of parameters (i.e. the number of weights no longer depends on the size of the input image) that need to be learned. An example of a 1D CNN is shown in Fig. 2 . At each layer, the input image is convolved with a set of K kernels $\mathrm{W} = \{ \mathbf{W}\,1 , \mathbf{W}\,2 , \ldots , \mathbf{W}\,K \}$ and added biases $\mathrm{B} = \{ b\,1 , \ldots , b\,K \}$, each generating a new feature map $\mathbf{X}\,k$. These features are subjected to an element-wise non-linear transform $\sigma(\cdot)$ and the same process is repeated for every convolutional layer l :

$$\mathbf{X}_k^l = \sigma\left(\mathbf{W}_k^{l-1} * \mathbf{X}^{l-1} + b_k^{l-1}\right).$$

The second key difference between CNNs and MLPs, is the typical incorporation of pooling layers in CNNs, where pixel values of neighborhoods are aggregated using a permutation invariant function, typically the max or mean operation. This can induce a certain amount of translation invariance and increase the receptive field of subsequent convolutional layers. At the end of the convolutional stream of the network, fully connected layers (i.e. regular

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neural network layers) are usually added, where weights are no longer shared. Similar to MLPs, a distribution over classes is generated by feeding the activations in the final layer through a softmax function and the network is trained using maximum likelihood.

Recurrent neural networks (RNNs)
Traditionally, RNNs were developed for discrete sequence analysis. They can be seen as a generalization of MLPs because both the input and output can be of varying length, making them suit- able for tasks such as machine translation where a sentence of the source and target language are the input and output. In a classification setting, the model learns a distribution over classes $P(y \mid \mathbf{x}1, \mathbf{x}2, \ldots, \mathbf{x}T;\_)$ given a sequence $\mathbf{x}1, \mathbf{x}2, \ldots, \mathbf{x}T$, rather than a single input vector $\mathbf{x}$. The plain RNN maintains a latent or hidden state $\mathbf{h}$ at time t that is the output of a non-linear mapping from its input $\mathbf{x}t$ and the previous state $\mathbf{h}t-1$:

$$\mathbf{h}_t = \sigma(\mathbf{W}\mathbf{x}_t + \mathbf{R}\mathbf{h}_{t-1} + \mathbf{b}),$$

where weight matrices $\mathbf{W}$ and $\mathbf{R}$ are shared over time. For classification, one or more fully-connected layers are typically added followed by a softmax to map the sequence to a posterior over the classes.

$$P(y|\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_T; \Theta) = \text{softmax}(\mathbf{h}_T; \mathbf{W}_{\text{out}}, \mathbf{b}_{\text{out}}).$$

Since the gradient needs to be back propagated from the out- put through time, RNNs are inherently deep (in time) and consequently suffer from the same problems with training as regular deep neural networks [32]. To this end, several specialized memory units have been developed, the earliest and most popular being the Long Short Term Memory (LSTM) cell [33]. The Gated Recurrent Unit [34] is a recent simplification of the LSTM and is also commonly used. Although initially proposed for one-dimensional input, RNNs are increasingly applied to images. In natural images 'pixelRNNs' are used as autoregressive models, generative models that can eventually produce new images similar to samples in the training set. For medical applications, they have been used for segmentation problems, with promising results [35] in the MRBrainS challenge.

Auto-encoders (AEs) and stacked auto-encoders (SAEs)
AEs are simple networks that are trained to reconstruct the in- put $\mathbf{x}$ on the output layer $\mathbf{x}\_$ through one hidden layer $\mathbf{h}$. They are governed by a weight matrix $\mathbf{W}x, h$ and bias bx, h from input to hid- den state and $\mathbf{W}h,x\_$ with corresponding bias $bh,x\_$ from the hidden layer to the reconstruction. A non-linear function is used to compute the hidden activation:

$$\mathbf{h} = \sigma(\mathbf{W}_{x,h}\mathbf{x} + \mathbf{b}_{x,h}).$$

Additionally, the dimension of the hidden layer $|\mathbf{h}|$ is taken to be smaller than $|\mathbf{x}|$. This way, the data is projected onto a lower dimensional subspace representing a dominant latent structure in the input. Regularization or sparsity constraints can be employed to enhance the discovery process. If the hidden layer had the same size as the input and no further non-linearities were added, the model would simply learn the identity function. The denoising auto-encoder [36] is another solution to prevent the model from learning a trivial solution. Here, the model is trained to reconstruct the input from a noise corrupted version (typically salt-and-pepper-noise). SAEs (or deep AEs) are formed by placing auto-encoder layers on top of each other. In medical applications surveyed in this work, auto-encoder layers were often trained individually ('greedily') after which the full network was fine-tuned using supervised training to make a prediction.

End-to-End learning (or training)
Often refers to the joint training of all parameters in a network such as the approach taken in Jia et. al. [31], Mortazi et. al. [32] and Sukhbaatar et. al.[33]. In neural networks, the input is accepted from one end, and the network produces an output at the other end. Training of parameters between these two ends (input to output) is called End-to-End training or learning.

A pre-trained network (transfer learning)
As the name implies, uses a network that has been previously trained with images and has optimized parameters for the task it will be performing. If a pre-trained network is used, then the parameters can be used for testing without the need for training the entire system, which can otherwise be a costly endeavor in terms of computation. Pre-training network will tend to work if the target task is similar to the base task (i.e. base task is the one that the network is trained and features are learned from). When the target data set is significantly smaller than the base data set, and the tasks are considerably different from each other (e.g. base network is trained to classify natural images while the target network is aimed to classify tumor images from mammography data), then the phenomena called **transfer learning** can be used to the transfer the knowledge from base task (i.e. features) into the target task.

III. HARDWARE AND SOFTWARE

One of the main contributors to the steep rise of deep learning papers has been the widespread availability of GPU and GPU- computing libraries (CUDA, OpenCL). GPUs are highly parallel computing engines, which have an order of magnitude more execution threads than central processing units (CPUs). With current hard- ware, deep learning on GPUs is typically 10–30 times faster than on CPUs. Next to hardware, the other driving force behind the popularity of deep learning methods is the wide availability of open-source software packages. These libraries provide efficient GPU implementations of important operations in neural networks, such as convolutions; allowing the user to implement ideas at a high level rather than worrying about efficient implementations. At the time of writing, the most popular packages were (in alphabetical order):

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•**Caffe** (Jia et al. [37]): Provides C++ and Python interfaces, developed by graduate students at UC Berkeley.
•**Tensorflow** (Abadi et al., [38]): Provides C++ and Python and interfaces, developed by Google and is used by Google research.
•**Theano** (Bastien et al., [39]): Provides a Python interface, developed by MILA lab in Montreal.
•**Torch** (Collobert et al., [40]): Provides a Lua interface and is used by, among others, Facebook AI research.
There are third-party packages written on top of one or more of these frameworks, such as Lasagne (https://github.com/Lasagne/ Lasagne) or Keras (https://keras.io/). It goes beyond the scope of this paper to discuss all these packages in detail.

IV. UNDERSTANDING BREAST CANCER DIAGNOSIS IN THE DEEP LEARNING

Machine learning algorithms (Naive Bayes, Genetic Algorithms, Fuzzy Logic, Clustering, Neural Networks, Support Vector Machines, Decision Trees and Random Forests etc.) have effectively been used for more than two decades for many purposes in breast cancer area such as detection, diagnosis, classification, and risk assessment. **Figure 1** supports a representative comparison of conventional machine learning models based CAD systems and deep learning based CAD systems, as each one of them use radiographic images for diagnosis breast cancer. The conventional machine learning method for image classification modeling is trained by well designed hand-engineered attributes (e.g. visual descriptions such as sphericity, or low gradients in borders) that are learned from radiologists. In contrast, deep learning depends on high-level imaging attributes supported from large sources/sets of images opened and available for training purposes. The literature pertaining to these machine learning algorithms, before the deep learning era, is vast. Interested researchers and individuals can refer to the literature [41-52] for further description of conventional machine learning methods in breast cancer, which include a large number of methods that are beyond the scope of this review.

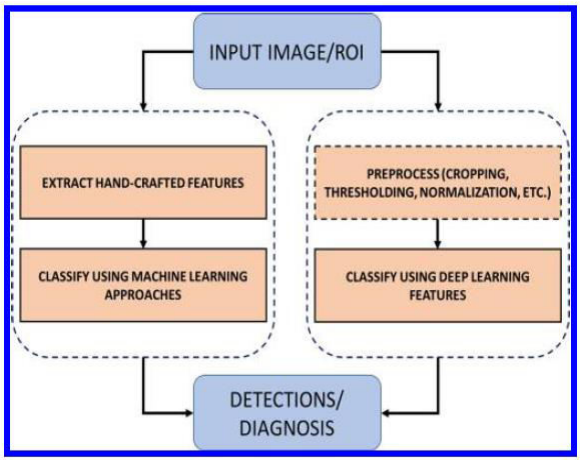

Figure 1: Comparison of conventional machine learning Approach vs deep learning based approaches, ROI, Region of interest.

V. BREAST CANCER IMAGING MODALITIES

In fact, many modalities are available for screening and detecting breast cancer. High numbers of works have been made for enhancing the breast cancer diagnosis accuracy via various imaging modalities. **Figure 2** presents the comparison between numbers of modalities in terms of effective radiation performed on the human body. The combined PET and CT give a better view of the suspect cells, however, the imaging techniques (such as CT and PET) reflect high radiation exposure to patients. Once these techniques are used for screening, the sheer amount of radiation the body is exposed to, while imaging may itself trigger cancer development. Thus, it is always preferable and recommended to use imaging techniques (mammogram and MBI) which have comparatively lower effective radiation.

Mammography

Mammography is a dedicated imaging modality for breast screening that uses low-dose X-ray during breast examination. Mammography is currently the most effective tool for early detection of breast cancer; however, it has some restrictions. Breast density is a variety of confounding factors that make diagnosis of breast cancer more difficult in women with dense breasts (Ertosun and Rubin, 2015[53]). The contrast between cancer and background in dense breast image is very low, which can affect the diagnosis outcome (Longo et al., 2014 [54]). In the mammographic examination, non-cancerous lesions can be misinterpreted as cancer (false-positive value), while cancers may be missed (false-negative value). As a result, radiologists fail to detect 10 % to 30 % of breast cancers (Bird et al., 1992[55]; Boyd et al., 2007[56]; Kerlikowske et al., 2000 [57]). The false-positive value indicates the percentage of lesions that are found to be cancerous and subjected to biopsy.

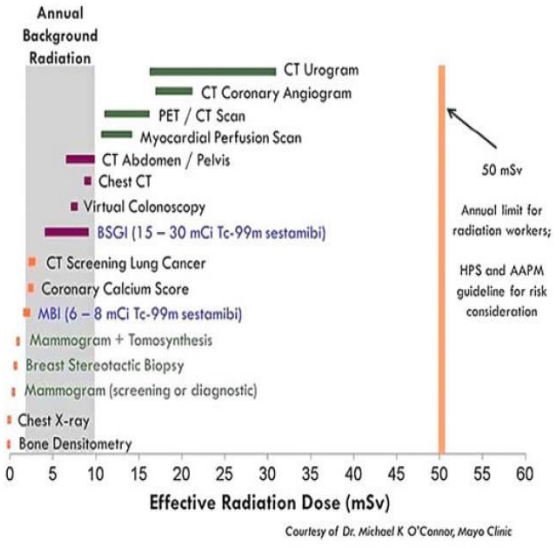

Figure 2: Effective various medical imaging modalities

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The miss rate in mammography has increased in dense breasts where the probability of cancer is four to six times higher than in non-dense breasts ([56]; [58]; [59]).
Several solutions have been proposed to enhance the specificity and sensitivity of mammography as well as to decrease unnecessary biopsies procedure. Double reading is one of the solutions that can significantly contribute to achieving high sensitivity and specificity ([60], [61]). Additional costs will be imposed on the patients for double reading of mammography. CAD systems can be considered as an alternative framework that acts as a second reader to enhance the performance of physician's interpretation.
The studies ([62]; 2011[63]; [64]; [65]) have shown that the attention to use a computer to improve the performance of physicians to detect mass and micro-calcification in mammography has increased in recent years. Gilbert et al. [66] indicated that proportion of cancer detected was 199 of 227 (87.7 %) for double reading and 198 of 227 (87.2 %) for single reading with CAD system. The perspective assessment of the impact of CAD systems on interpretation mammogram images has been performed on a community of breast cancer patients [67]. Among 12,860 mammograms, the radiologist's performance was measured without CAD and with CAD. The recall rate increased from 6.6 % to 7.7 % and the proportion of early-stage malignancy detected the growth from 73 % to 78 %, which represents an increase in efficiency in the detection of cancer with the usage of CAD system. Micro-calcifications and masses are the two most significant signs of malignancy. Breast calcification is tiny specks of calcium which are scattered in the breast. In order to classify micro-calcification in benign and malignant, different properties such as size, shape, distribution pattern, density, and a number of micro-calcifications are analyzed [68]. Detection of microcalcifications is a difficult task and the hardship increases in mammogram interpretation in young women due to the contrast reduction among micro-calcification and adjacent tissue [69]. Authors in [70] have provided a valuable study on techniques for suppressing noise, enhancing contrast, and extraction; and classification of micro-calcification. Another lesion in the breast is mass, which; is a circumscribed lump in the breast and might be categorized to be benign or malignant. Masses are characterized by various attributes such as shape (round, lobular, oval, irregular), margin (obscured, indistinct, and speculated), size, location, and their contrast. Mass detection is more difficult compared to micro-calcification because of the similarity and ambiguity of their characteristics with the normal tissue [71]; [72].
Masses are generally observed in the dense regions of the breast with smoother boundary rather than micro-calcification ([72]). Due to these factors, mass detection is a challenging task for radiologists. In the past two decades, researchers have conducted a lot of effort for developing automatic systems to help radiologists in the detection and diagnosis of mass on mammography image. Oliver et al. [73] have presented an exhaustive study of CAD systems for the detection and segmentation of mass from mammogram images. In this study, the introduction of current systems for mass detection and the used strategies as well as a quantitative comparison of a few methods are provided. Although mammography is a proven modality for mortality reduction in breast cancer, one of the noteworthy points is low sensitivity and specificity in young women and dense breast ([56]; [58]; [59]). Low specificity in screening mammography may cause some unnecessary biopsy [74]. This restriction increases the cost and stress imposed on the patient. Consequently, to gain high precision in mammography screening alone is difficult. Some observational studies have shown improve screening sensitivity in women with dense breast, through adjunct mammography with ultrasound ([75]; [76]; [77]; [78]; [79]; [80]).

Ultrasound

Ultrasound is a beneficial tool to evaluate breast issues and to follow up finding in physical exam or mammography. It is also recommended for breast screening during pregnancy and lactation. Ultrasound is suggested before diagnostic fine needle biopsy and it can be used for biopsy guidance and mass locating. Although ultrasound is less sensitive than MRI, it has converted a valuable tool as an adjunct to mammograms due to its availability, non-invasive, and costs effective than other options. The development of colour Doppler imaging and ultrasound echo-enhancing (contrast agents) provides additional information of anatomical and vascular flow related, which assists the differential diagnosis of breast lesions [81]. The studies indicate that ultrasound is able to detect and discriminate benign and malignant masses with high accuracy and also reduce the number of unnecessary biopsies [82]; [83].
Ultrasound is more sensitive for detecting invasive cancer in dense breasts [84]; [85]. However, it is an operator-dependent modality and the interpretation of its images requires expertise on the part of the radiologist. In order to overcome the operator dependency and increase the accuracy of diagnosis rate, computer-aided detection/diagnosis (CAD) systems are developed for breast cancer detection and classification on ultrasound images. Recently, several CAD systems have been proposed to reduce the influence of dependence on the operator in ultrasound and increase the diagnosis sensitivity and specificity [86]; Kim et al., 2014[87]). CAD systems have been presented on Automated Breast Ultrasound (ABUS) (Kim et al., 2014[87]).
The CAD system is evaluated on a dataset that involves 20 cysts, 42 benign lesions, and 27 malignant lesions. The sensitivity achieved by this system was 82.67 percent and the false positive rate was 0.26 per image. The efficiency of CAD software is generally higher to detect lesion with a high risk of malignancy in contrast to the benign lesion [89]. Ref. [88] have presented the results of ultrasound image analysis with and without CAD system by junior radiologists to detect breast cancer. With the high sensitivity (95 %) and low specificity (48 %) achieved in this research, it appears that CAD system is a useful tools

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for image interpretation for the junior radiologist in training.

Magnetic Resonance Imaging (MRI)
Since nearly three decades, MRI screening has been employed for detection and diagnosis of breast cancer lesions (Heywang et al., 1989 [90]). Breast MRI is a potential alternative, but the cost is higher than other imaging methods and not widely available as ultrasound and mammography. MRI is suggested for screening women who have a high risk of developing breast cancer, or it can be used to investigate suspicious areas found by the mammogram to help measure the size of the mass. Breast MRI is advised to women with family history of breast cancer and has a high rate of sensitivity (78-98 %) and low specificity (43-75 %) [91]. The interpretation process of MRI image is very time-consuming and requires a high level of radiologist experience to detect and differentiate benign and malignant lesions [92]. In recent studies, computer systems have been developed to facilitate MRI image analysis and improve the diagnosis productivity ([92]; [93]; [94]).

Biopsy
Biopsy is the final stage when a mammogram or other imaging modalities found any type of abnormality. During a biopsy, a sample is taken from suspicious lesion in order to conduct microscopic observation. There are several types of biopsies such as fine needle aspiration biopsy (FNAB), core biopsy, or surgical biopsy. FNAB is a common type of biopsy and during the examination; a cytological sample is obtained from the tumour and explored under a microscope to determine the occurrence of cancer cells. The main disadvantage of FNAB is that the needle cannot extract sufficient amount of tissue for diagnosis. Detection of cancer cells requires profound knowledge and sufficient experience in the field of histopathology (Filipczuk et al., 2012[95]). A vision-based computer system to automatically detect the cancer cells can help specialists to discriminate cancer from non-cancer cells. In contrast to other CAD systems, fewer studies performed the analysis of breast histopathology images. Issac Niwas et al. (2012[96]) have used Log-Gabor wavelet transform base decomposition method for histopathological images on HSV (Hue, Saturation, Value) colour space. The accuracy obtained by Least squares Support Vector Machine (LS-SVM) in this study was 98.3 %. Another study has applied the Genetically Optimized Neural Network (GONN) algorithm for diagnosis on histopathology images (Bhardwaj and Tiwari, 2015[97]). They achieved an average accuracy of 97.73 %, 99.11 %, and 99.21 % for 50-50, 60-40 and 70-30 training-testing partitions respectively, and 99.26 % for 10-fold cross validation structure.

Computed tomography (CT)
The benefits of diagnostic computed tomography appear to be small, as it is of high cost and has the potential for high exposure of radiation. Therefore, its indications are very limited.

Nuclear medicine breast imaging
Technetium-99 sestamibi has been found to concentrate in some breast cancers. However, its role in breast cancer evolution has yet to be defined, because it cannot be used to differentiate benign lesions from malignant ones and its efficacy remains to be defined.

Positron emission tomographic screening (PET)
Early studies suggested that breast cancers have elevated metabolic activity, which can be detected using fluorine 18-labeled glucose. PET may be a method for staging breast cancers and for assessing the possibility of recurrence after initial breast cancer treatment. The use of PET as a diagnostic technique to differentiate benign from malignant lesions and to reduce the need for needle aspiration biopsies is still under study.

Breast mass evaluation
When a mass is found as part of the screening process, the histological type of the cancer should be determined. The first step is to determine whether the mass is solid or cystic, often accomplished through a needle aspiration biopsy, using a needle or syringe. If cystic fluid (non-bloody serous fluid) is found, the patient is recommended to return for a follow-up re-evaluation in four to six weeks. However, if the mass is not cystic, then a fine needle aspiration should be performed. If the fine needle aspiration is inconclusive or negative, an open biopsy must be performed.

VI. CORNERSTONES OF A CAD SYSTEM

Medical image processing requires prior knowledge on the content and nature of image to select appropriate methods to implement the CAD system. In order to achieve a high level of efficiency for automated diagnosis, it is significant to employ efficacious image processing approaches in the main steps of CAD system. Commonly, the CAD system consists of four stages as shown in **Figure 3**.

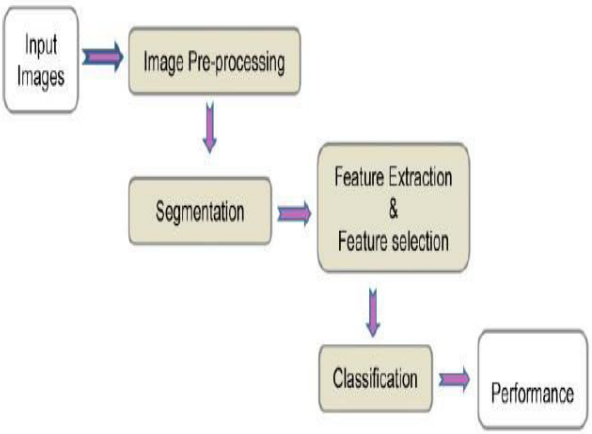

Figure 3: the main steps of CAD system

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A brief description of the main stages of a CAD system is provided as follows:

1. **Image pre-processing:** This step is essential for some modality such as ultrasound for the purpose of enhancing the image and reducing the noise with minimum distortion of image features. Some of the CAD systems do not have a pre-processing stage.
2. **Image segmentation:** Image segmentation is a vital step towards efficient development of CAD systems. The main purpose of segmentation is the separation of the region of interest (ROI) commensurate with the desired properties [**98**]. Recently, imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), 3D ultrasound, and many more modalities are capable of producing images in the form of 3D. Therefore, 3D segmentation methods are desirable for more accurate segmentation in volumetric imagery.
3. **Feature extraction and selection:** In this step, different features are extracted according to the characteristics of lesions from the image. These features are used to distinguish benign or malignant lesions. The feature set is usually very large and the selection of the most effective features is very critical for the next step.
4. **Classification:** According to the selected features, the suspicious areas are classified to benign or malignant based on different classification techniques. The common classification methods used in medical imaging are presented in this section.
5. **Performance evaluation:** This step evaluates the performance of CAD system.

VII. OPEN SOURCE DATASET ACCESS AND QUALITY

Researchers have access to several public and restricted image databases. However, quantity, quality, and availability of metadata and clinical data vary a lot between those datasets. For example, scanned hard copy films may not be useful for developing state-of-the-art digital mammography algorithms. One of the more popular databases is DDSM which is available to the general public containing more than 10,000 images. Unfortunately, the quality of the digitized films does not match that of FFDM [99] and the provided annotations are not as accurate as they should be for training machine learning systems (e.g., 339 images contain annotations although the masses are not clearly visible [100]). An up-to-date and better curated version of DDSM was published more recently [100]. At the time of writing, only one group has published work on the new release of DDSM [101]. The second most frequently cited database is MIAS, however, compared to DDSM it lacks samples.

Furthermore, offering only 8-bit images is no longer state of art; therefore we can only assume that this dataset will not be useful for future deep learning projects. The In Breast dataset is also often used as a benchmark as it consists of annotated FFDM images. However, with 115 cases it is rather small, cannot be considered representative of real-world inputs, and is not suitable to assess the performance of algorithms in real-world settings. There are many other mammography datasets, with varying volume and quality. **Table 1** summarizes the most popular of these publicly available data sources.

VIII. REVIEW FOR DEEP LEARNING TECHNIQUES FOR BREAST IMAGE ANALYSIS

One of the earliest DNN applications from Sahiner et al. [102] was on breast imaging. Recently, interest has returned which resulted in significant advances over the state of the art, achieving the performance of human readers on ROIs [103]. Since most breast imaging techniques are two dimensional, methods successful in natural images can easily be transferred. With one exception, the only task addressed is the detection of breast cancer; this consisted of three subtasks: (1) detection and classification of mass-like lesions, (2) detection and classification of micro-calcifications, and (3) breast cancer risk scoring of images. Mammography is by far the most common modality and has consequently enjoyed the most attention. Work on tomosynthesis, US, and shear wave elastography is still scarce, and we have only one paper that analyzed breast MRI with deep learning; these other modalities will likely receive more attention in the next few years. **Tables 2** summarized the literature and main messages.

Table 1: public data sources

Name	Origin	Year	No. of cases	No. of images	Access
MIAS	UK	1994	161	322	Public
OPTIMAM	UK	2008	9559	154,078	On request
DDSM and CBIS-DDSM	USA	1999	2620	10,480	Public
Nijmegen	Netherlands	1998	21	40	On request
Trueta	Spain	2008	89	320	On request
IRMA	Germany	2008	Unknown	10,509	Public
MIRAcle	Greece	2009	196	204	Unknown
LLNL	USA	Unknown	50	198	Cost
Malaga	Spain	Unknown	35	Unknown	Unknown
NDMA	USA	Unknown	Unknown	1,000,000	On request
BancoWeb	Brazil	2010	320	1400	Public
Inbreast	Portugal	2012	115	410	On request
BCDR-F0X	Portugal	2012	1010	3703	On request
BCDR-D0X	Portugal	2012	724	3612	On request
SNUBH	Korea	2015	Unknown	49	Public

Since many countries have screening initiatives for breast cancer, there should be massive amounts of data available, especially for mammography, and therefore enough opportunities for deep models to flourish. Unfortunately, large public digital databases are unavailable and consequently older scanned screen-film data sets are still in use. Challenges such as the recently launched DREAM challenge have not yet had the desired success. As a result, many papers used small data sets resulting in mixed performance. Several projects have addressed this issue by exploring semi-supervised learning [104], weakly supervised learning [105], and transfer learning [106]; [107]. Another method combines deep models with handcrafted features [108], which have been shown to be

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complementary still, even for very big data sets [103]. State of the art techniques for mass-like lesion detection and classification tend to follow a two-stage pipeline with a candidate detector; this design reduces the image to a set of potentially malignant lesions, which are fed to a deep CNN [109]; [103] . Alternatives use a region proposal network (R-CNN) that bypasses the cascaded approach [110]. When large data sets are available, good results can be obtained. At the SPIE Medical Imaging conference of 2016, a researcher from a leading company in the mammography CAD field told a packed conference room how a few weeks of experiments with a standard architecture (AlexNet) –trained on the company's proprietary database –yielded a performance that was superior to what years of engineering handcrafted feature systems had achieved [109].

Table 2: Overview of papers using deep learning techniques for breast image analysis

No.	Studies	Application	Imaging Modality	Deep Learning Technique	Training	Open Source Dataset
1	Carneiro et al. [111]	Mass Detection	Mammographic	CNN	End-to-end	Unpublished dataset
2	M. G. Ertosun and D. L. Rubin [112]	Mass Detection	Mammographic	CNN	End-to-end	DDSM [113]
3	W. Zhu [114]	Mass Classification	Mammographic	CNN	End-to-end	MIAS [115]
4	I. Domingues and J. S. Cardoso [116]	Mass Detection	Mammographic	CNN	End-to-end	DDSM [113]
5	N. Dhungel et al. [117]	Mass Detection	Mammographic	CNN	End-to-end	Unpublished dataset
6	B. Q. Huynh [118]	Mass Lesion Classification	Mammographic	CNN	Transfer learning	DDSM [113]+ Inbreast [119]
7	D. L´evy & A. Jain [120]	Mass Lesion Classification	Mammographic	CNN	End-to-end	Banco Web[121]
8	J. Arevalo et al. [122]	Mass Lesion Classification	Mammographic	DCN	End-to-end	FFDM [160]
9	J. Mordang et al. [123]	Micro-classification Detection	Mammographic	CNN	End-to-end	Unpublished dataset
10	J. Wang et al. [124]	Mass Classification	Mammographic	CNN	End-to-end	MIAS[115]
11	J. Bekker et al.[125]	Mass Classification	Mammographic	CNN	End-to-end	DDSM [113]
12	J. Arevalo [126]	Mass Lesion Classification	Mammographic	CNN	End-to-end	BCDR [127]
13	K. Sharma & B. Preet [128]	Classification	Mammographic	DCN	End-to-end	DDSM [113]+ INbreast[119]
14	A. Dubrovina [129]	Multi-Region Segmentation & Tissue Classification	Mammographic	CNN	End-to-end	Unpublished dataset
15	X. Pengcheng et al. [130]	Mass Classification & Localization Of Abnormalities	Mammographic	CNN	End-to-end	MIAS [115]
16	S. Karthik et al. [131]	Mass Classification	Mammographic	DCN	End-to-end	WBCD
17	A. Rakhlin1 et al. [132]	Mass Classification	Histopathology	CNN	End-to-end	MITOSATYPIA-14 [133]
18	A. Jamieson [134]	Mass Classification	Mammographic & Ultrasound	AND	End-to-end	DDSM[113]
19	Albayrak et al. [135]	Mitosis detection	Histopathology	CNN	End-to-end	MITOSATYPIA-14 [133]
20	Spanhol et al. [136]	classification	Histopathology	CNN	End-to-end	BreaKHis [137]
21	Chen et al. [138]	Mitosis detection	Histopathology	FCN+CNN	Transfer learning	MITOSATYPIA-14 [133]
22	Albarqouni et al. [139]	Mitosis detection	Histopathology	CNN	End-to-end	MITOSATYPIA-14 [133]
23	Xu et al. [140]	Nuclei classification	Histopathology	SSAE	End-to-end	Unpublished dataset
24	Wichakam et al.[141]	Mass detection	Mammographic	CNN	End-to-end	INbreast [45]
25	Suzuki et al.[142]	Mass detection	Mammographic	CNN	Transfer learning	DDSM [46]

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Table 2: Overview of papers using deep learning techniques for breast image analysis

No.	Studies	Application	Imaging Modality	Deep Learning Technique	Training	Open Source Dataset
26	Swiderski et al. [143]	Lesion recognition	Mammographic	CNN	End-to-end	DDSM [46]
27	Ertosun et al. [144]	Mass segmentation	Mammographic	CNN	End-to-end	DDSM [46]
28	Kallenberg et al. [145]	segmentation & risk scoring	Mammographic	SSAE	End-to-end	FFDM [160]
29	Dhungel et al. [146]	Mass segmentation	Mammographic	DBN	End-to-end	DDSM [46] + INbreast[45]
30	Dhungel et al.[147]	Mass detection	Mammographic	DBN+CNN	End-to-end	DDSM [46]
31	Kim et al.[148]	Latent bilateral feature	Tomosynthesis	CNN	End-to-end	Unpublished dataset
32	H. Chougrad [149]	Mass detection	Mammographic	CNN	End-to-end Transfer learning	DDSM + BCDR + INbreast
33	S. Wenqing et al. [150]	Mass detection	Mammographic	CNN	End-to-end	FFDM [160]
34	D. Selvathi [151]	Mass detection	Mammographic	CNN	End-to-end	mini-MIAS
35	Pablo Guill´en-Rondon [152]	Breast cancer Classification	microscopic biopsy	CNN	End-to-end	BreakHis[137]
36	Dan C. Cires et al. [153]	Mitosis detection	microscopic biopsy	DNN	End-to-end	Unpublished dataset
37	Ming Fan et al.[154]	Mass detection	Tomosynthesis	CNN	End-to-end	Unpublished dataset
38	Dongdong et al. [155]	prognosis prediction	Mammographic	DNN	End-to-end	METABRIC [156]
39	Krzysztof et al. [157]	Breast Cancer Prediction	Mammographic	CNN	End-to-end	Unpublished dataset
40	Kooi et al. [158]	Mass Detection	Mammographic	DCN	End-to-end	DDSM [46]
41	Becker et al. [159]	Mass Detection	Mammographic	DCN	End-to-end	Unpublished dataset
42	A. Ballin et al. [110]	Mass Detection & Classification	Mammographic	DCN	End-to-end	DDSM [46]
43	Dalmis et al. [161]	Breast and fibroglandular tissue segmentation	Mammographic	CNN	End-to-end	Unpublished dataset
44	Samala et al. [107]	CNN on mammographic masses transferred to tomosynthesis	Tomosynthesis	CNN	End-to-end	DDSM [46] + INbreast[45]
45	Sun et al. [104]	Mass Classification	Mammographic	CNN	End-to-end	DDSM [46]
46	Hwang and Kim [105]	masses localization	Mammographic	CNN	End-to-end	DDSM [46]
47	Kisilev et al. [162]	semantic descriptions of potential masses	Mammographic	CNN	End-to-end	Unpublished dataset

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IX. SUMMARY AND DISCUSSION

Literature on deep learning-based breast cancer detection from mammography shares very similar network designs: pre-trained network, data augmentation (or transfer learning), and extracting features to be used with classifiers such as support vector machine, random forest, or others. In other words, deep networks were used only for extracting discriminative features (*i.e.* imaging features that are unique to tumor type). The use of pre-trained networks for breast cancer diagnosis started in 2015. Most pre-trained networks are trained on the *ImageNet* data set owing to a large number of images (>1 million) and thousands of classes. Several studies showed that pre-trained models could be used to boost classification results for mammograms. However, there is no consensus on what features should be used for classification. The only study, to our knowledge, that puts some sort of feature interpretations into the diagnostic task is by Becker et al [159]. Uniquely, the authors studied the relationship of breast density to classification accuracy and found that low density was easier to classify.

Among the 47 surveyed papers on breast cancer, 6 studies were focused on cancer diagnosis based on digital pathological images, 36 studies were focused on cancer detection based on mammograms, two studies was focused on cancer detection with microscopic biopsy and 3 studies was focused on cancer detection with Tomosynthesis. For the papers on cancer detection based on mammograms, the open source databases were used such as: MIAS [115], INbreast [45], Banco Web [121], BreakHis [137] and DDSM [46]. Note that 37 of 47 surveyed papers used open source databases; the rest of papers tested and evaluated their methods on the datasets collected from medical organizations, such as medical universities, hospitals, and cancer research centers. The lack of large training data in the open source datasets was probably the main reason why those papers chose to use clinical data. Another possible reason is that the information, except images data, provided by open source datasets was limited for some specific applications.

Among all 47 studies surveyed in this paper, 34 studies adopted CNN models, 6 studies adopted DCN models, 2 studies adopted SSAE models, 2 studies adopted DNN models, 1 study adopted DBN model and 2 studies proposed hybrid model based on multiple types of deep learning models FCN & CNN. Each study and the corresponding deep learning methods being used in the paper are listed in Tables 2. Comparison results show that CNN has been widely studied and adopted for different types of cancer detection tasks.

X. DISCUSSION AND FUTURE DIRECTIONS

From the surveyed papers, we found that one big challenge of training deep learning models for medical image analysis was the lack of large training datasets. Although the popularization of picture archiving and communication system (PACS) in hospitals has helped gather millions of medical images, most of them include confidential information of patients and they are stored in hospitals. In order to make those datasets available for research uses, more efforts are needed on those data, such as de-identification and data transportation. Many surveyed papers used different datasets collected from hospitals or cancer research organizations to test and evaluate deep learning models. The main drawback is that it is difficult to compare the performance of deep learning models among different studies. Open source medical image datasets have been provided for public research on different types of cancers in recent years. However, it is worth noting that, for some types of cancer research, the number of case studies (patients) in the dataset is too small [163]. In addition, some of open source datasets only contained raw image data, extra efforts from expert domain are required to generate ground truth for the purpose of the model training as well as evaluation. Therefore, it is desirable to build up larger and more systematic open source datasets for different applications.

Another problem about the medical image dataset is that the ratio of positive and negative in the dataset is often heavily imbalanced. Training models directly on imbalanced data may bias the prediction towards the more common classes. We found that most studies ignored this problem in the training stage.

Another big challenge using CNN models for cancer detection was the size variation of target objects within the images. To overcome this problem, several studies proposed to train the same CNN models using different scales of image data, and fused the outputs of multiple models to gain final result [139, 145 and 108]. I note that there is a lack of studies to compare the performance and efficiency of different methods. It is desirable to develop approaches robust to the size variation of target objects.

The studies surveyed in this review used different datasets as well as different imaging modalities, thus it is difficult to conduct a comparison on the performance of all the methods (specificity and sensitivity) with clinical standard practice for cancer diagnosis. However, the ground truth of most datasets are provided through expert consensus or pathology report information, therefore it is reasonable to rely on the evaluation results to demonstrate the potential of deep learning algorithms for cancer detection and diagnosis.

In summary, deep learning has shown a significant improvement compared with many other machine learning methods in different applications. The success of deep learning in natural scene image classification and segmentation stimulates the research of adopting it in image-based cancer detection and diagnosis. One major advantage of deep learning is that it reduces the need of feature engineering, which is one of the most complicated and time-consuming parts in machine learning practice, especially in processing redundant image data. In addition, it is relatively easy to adapt or modify existing deep learning architectures on new applications. However, it is worth noting that there are also some disadvantages in adopting deep learning in real practice: (1) deep learning models often require a large amount of training data to achieve superior performance than other methods. (2)

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Training process is extremely computational expensive and it is quite time consuming to train a deep and complex model even with the support of most powerful GPU hardware. (3) The body of trained deep learning model is like a black box, we still lack the perfect methodology to fully comprehend its deep structure.

XI. CONCLUSION

In this paper, we surveyed most recent studies on the subject of applying deep learning techniques in image based cancer detection and diagnosis. This application is organized depending upon specific type of cancer, which is “breast cancer”. Six popular Images based deep learning models, including Convolutional neural networks, fully convolutional networks and deep belief networks are highlighted in the survey. The uniqueness of past studies and some potential topics for future study are discussed.

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