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REVIEW ARTICLE

Intensive Training in Breast Imaging With Artificial Intelligence and Deep Learning- A Review Article

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ABSTRACT

To lower breast cancer morbidity and mortality, millions of breast imaging tests are carried out year. Breast imaging tests are carried out for cancer screening, diagnostic evaluation of suspicious findings, assessing the severity of the illness in patients who have just been diagnosed with breast cancer, and assessing treatment response. However, the interpretation of breast imaging can be arbitrary, laborious, slow, and open to human error. Deep learning (DL) has a great potential to perform medical imaging tasks at or above human-level performance, and may be used to automate parts of the breast cancer screening process, increase cancer detection rates, reduce needless callbacks and biopsies, improve patient risk assessment, and create new opportunities for disease prognostication. Retrospective and small reader studies support this claim. In order to verify these suggested tools and open the door to actual therapeutic application, prospective studies are urgently required. To meet the distinct ethical, medico legal, and quality control challenges that DL algorithms provide, new regulatory frameworks must also be created. In this paper, we cover the fundamentals of DL, present current DL breast imaging applications, such as cancer diagnosis and risk prediction, and talk about the difficulties and potential paths for AI-based breast cancer systems.

Keywords: *Deep Learning (Dl), Artificial Intelligence, Breast Imaging, Digital Breast Tomosynthesis and Mammography*

INTRODUCTION

The area of medical imaging offers significant potential for change because to artificial intelligence (AI). Recent developments in computer algorithms, expanded computing availability power, and more people having access to large data, are this uprising. AI software may be trained to extract huge data sets with patterns, including sets with a large number of medical photos, and they can meet, even go beyond, human-level performance over a range of repeating well specified tasks. The development of AI algorithms is particularly well suited for breast imaging since the diagnosis problem is simple and data is widely available. The majority of breast imaging tests are binary classification issues (e.g., malignant vs. benign), and practically all studies include a ground truth that is generally available for use during algorithmic development (e.g., histology or negative imaging follow-up). Additionally, population-wide screening programmes have made standard imaging data widely accessible, and the American College of Radiology (ACR) Breast Imaging and Reporting Data System (BI-RADS) system requires organised reporting and evaluations. To date, retrospective and small reader studies have demonstrated that AI technologies may be used to predict treatment response, enhance breast cancer risk assessment, improve diagnostic accuracy, and perform other jobs. AI is also being used to enhance image reconstruction generally, allowing for the acquisition of high-quality pictures in MRI and mammography procedures with less radiation exposure and shorter scan periods. AI is in a unique position to assist breast imagers at both interpretative extremes. On the one hand, AI may be used to automate straightforward activities, such as eliminating entirely normal examinations from the radiology work list so radiologists can focus on more difficult patients. Computer algorithms are ideally suited for simple repetitive operations that people may find monotonous or tiresome since they do not get tired or distracted. However, AI has the potential to expand the boundaries of medical practise. AI is able to spot intricate patterns in imaging data that are invisible to the human eye, providing a wealth of knowledge that makes it possible to model diseases more accurately and personalise treatment plans. The generalizability of results is constrained by the fact that nearly all research conducted to far have been retrospective trials or small reader studies. Prospective studies are now required to more thoroughly assess these AI technologies' performance and are a requirement for responsible clinical translation. The principles of artificial intelligence (AI) and deep learning will be covered in this article, along with a variety of AI applications in clinical breast imaging. We'll also discuss challenges and possible directions for future study.

Deep Learning and Artificial Intelligence

Computer-aided detection (CAD) software for mammography was created in the 1990s and 2000s using traditional machine learning, a branch of artificial intelligence. Initial studies [18] showed that CAD increased diagnostic precision; it was approved by the FDA in 1998 and saw widespread adoption during the ensuing 18 years [19]. But more recent, bigger trials showed that CAD produces a lot of false positives and does not increase diagnostic accuracy, therefore it has mostly lost popularity. When AlexNet decisively defeated the competition in the Image Net Large Scale Visual Recognition Challenge in 2012, deep learning (DL), a new kind of representational machine learning, initially attracted notice [21]. An enormous amount of work has been put towards using DL in diagnostic radiology, and breast imaging in particular, since 2016. [22, 23] without consulting experts, DL models determine which imaging characteristics are necessary to conduct this classification in addition to classifying input pictures as positive or negative [24]. In contrast, classic machine learning methods (such as CAD) rely on manually created characteristics (such as shape and margin) to conduct categorization (Figure 1a). This significant distinction explains why modern DL algorithms outperform conventional machine learning approaches (if there is enough data available). Convolutional neural networks are typically used in DL algorithms for medical imaging (CNN). In order to extract hierarchical patterns from data, CNNs need millions of weights (i.e., variables to be optimised) and numerous levels of processing. The majority of deep learning (DL) models for medical imaging employ supervised learning, which calls for extensive usage of labelled training data.

Data labelling can be done at various levels, including the exam level (for example, the entire mammogram exam can be classified as benign or malignant), the breast level (for example, the left breast can be classified as benign while the right breast is classified as malignant), the pixel level (for example, the area of malignancy can be circled), and anywhere in between. Despite being expensive to produce, pixel-level labelling provides the most details and decreases the amount of training data that must be used. A general purpose learning procedure 24 is utilised during CNN training to concurrently and autonomously execute feature selection and classification (Figure 1b). Numerous tagged medical pictures are delivered directly into a CNN during training. The top layer picks up on tiny, straightforward features (such the position and orientation of edges), the next levels pick up on specific combinations of those simpler features, and the deeper layers pick up on even more intricate configurations of those earlier patterns. The last layers categorise the image or look for other interesting patterns using these imaging attributes or representations (Figure 1b). A held-out test set that wasn't utilised during training is used to evaluate a CNN's performance after it has been completely trained. Ideally, a data set is used to further validate CNN's performance. Since DL approaches are data-driven, outcomes often get better as data set size rises. Although training data sets must be sufficiently wide and diverse to include the range of phenotypes of the categories that they intend to categorise, there is no established formula for determining the number of data sets required to train a model for a given job. When building a large enough data set to train a CNN from scratch is not doable CNN weights (a common occurrence in medical imaging). Initialised using weights acquired from a previous job (For instance, categorising cats and dogs). This method of transfer

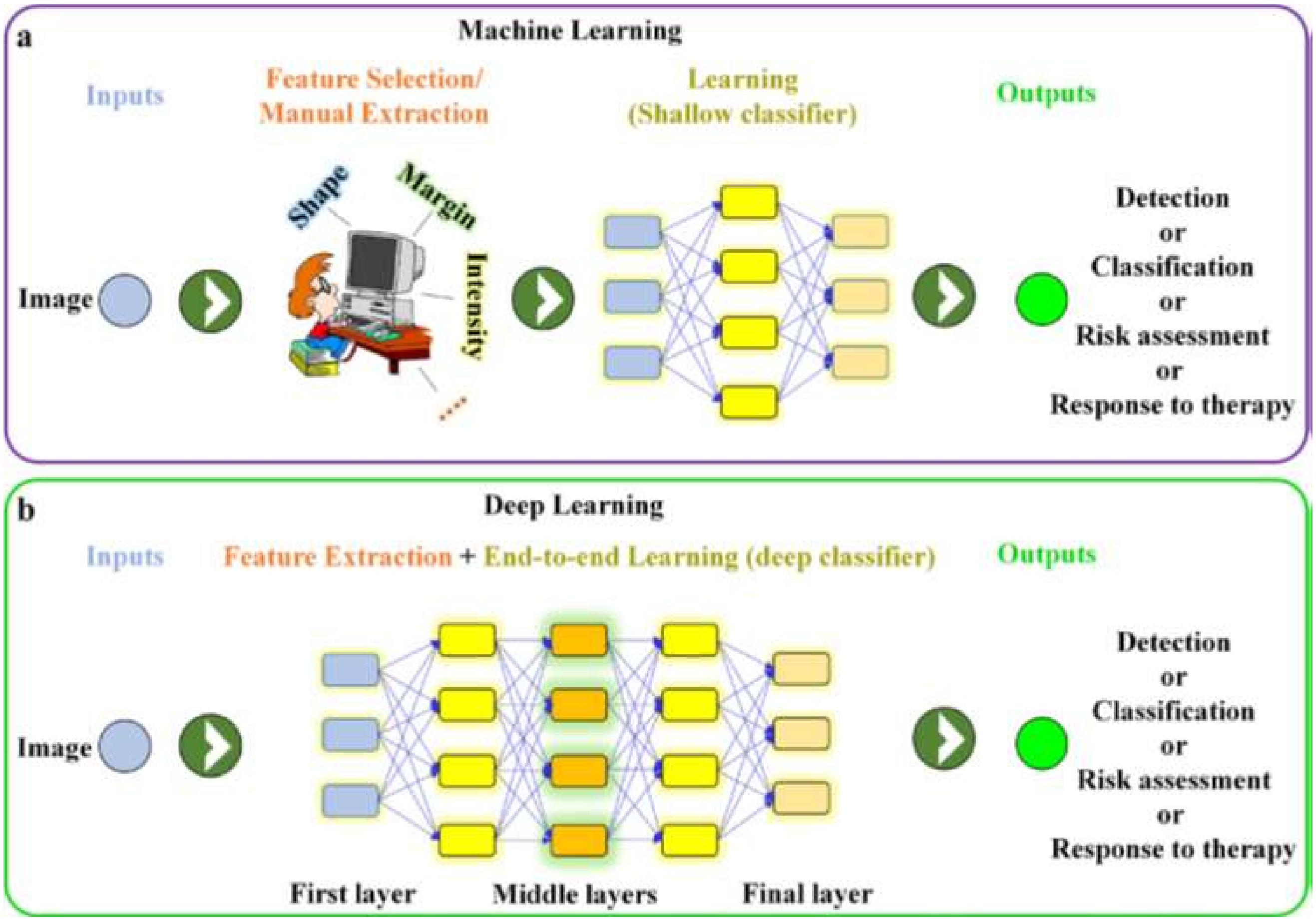


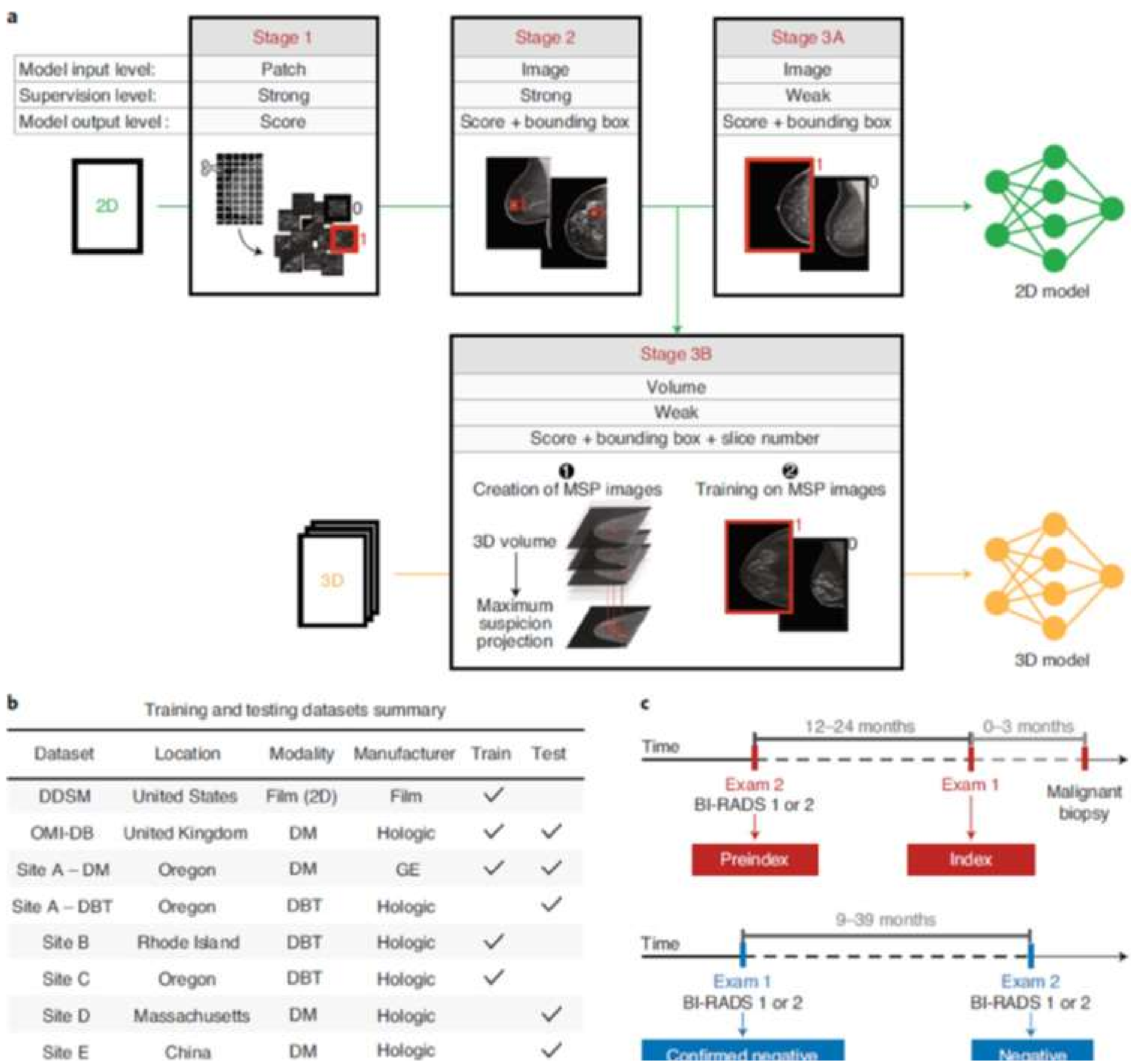
Figure 1: shows a schematic of an end-to-end deep learning network and a feature-based (human-engineered) machine learning network (e.g., using traditional CAD software). Computer-aided design, or CAD

learning lowers the amount of the required data sets for CNN training [24,26].

Digital Breast Tomosynthesis And Mammography Research On Cancer Categorization And Detection

Breastcancerisdiagnosedinmorethan 300,000 people annually in the United States alone. Mammography for screening reduces breast cancer mortality by 20–35%; however it is not a perfect technology [27]. Even among breast imaging specialists, there is substantial variation in the sensitivity and specificity of mammography, which range from 67 to 99 percent and [71 to 97] percent, respectively. 28 DL has the potential to boost these KPIs by lowering needless callbacksandraisingcancerdetectionrates. Numerous reader and retrospective studies have previously demonstrated that AI models perform as well as or better than experienced radiologists [9,22,29-31]. Reader studies have combined general radiologists, fellowship-trained breast imagers, and occasionally even trainees, which is crucial to take into account when asserting the superiority of one method over another. It's important to highlight that whereas early DL experiments relied on 2D mammography, more recent research has concentrated on DBT [7,29,32,33] which is a more difficult technical challenge but has the potential to enhance AI performance even more. DBT is more time-consuming for radiologists to interpret than 2D mammography by around 50%,34 therefore AI solutions for DBT are being developed with clinical efficiency in mind rather than only to discover more tumours. Lotter et al. introduced a DL model for cancer detection that produced state-of-the-art performance for mammographic classification, demonstrating an area under the curve (AUC) of 0.945 in their retrospective analysis, in one of the most significant AI mammography/DBT investigations to date. 29 The DL model shown strong generalizability by outperforming five experienced breast imagers in a reader study, working for both 2D digital mammography and 3D DBT, and receiving external validation utilising imaging data from several national and one international location **(Figure 2).** Using a single standardised data set, independently assessed the performance of three commercial AI systems for mammography screening [35] Combining one of the three AI algorithms with a human reader produced results that were superior to those of the human readers. Prospective clinical studies are required to open the door for clinical translation. The majority of these studies, which are presently accepting applicants, are testing how well the commercial AI software programmes Transpara (Screen Point Medical) and INSIGHT MMG (Lunit) perform in various clinical and geographical contexts. For instance, the ScreenTrust CAD trial (NCT04778670) will compare the Lunit software to single and double readings by radiologists, while the AITIC trial (NCT04949776) will assess whether Transpara can reduce the workload of a breast screening programme by 50% with non-inferior cancer detection and recall rate.

Figure 2 shows a multistage deep learning model's data summary and training. 29 (A) A stage-by-stage illustration of model training Stage 1 provides a patch-level classification example. Stage 2 shows an intermediate phase where bounding boxes and likelihoodratings formalignancy were identifiedusing complete mammography pictures and a detection-based model. In Stage 3A, the detection-based model is retrained using a multi-instance learning methodology, computing the maximum score across all bounding boxes in each entire mammography image to determine whether or not there is cancer present. A similar detection-based model for DBT was trained in Stage 3B utilising maximum suspicion projection images. (a) A summary of the training and testing data sets from multiple institutions. (c) An example of an exam definition that was used in the research [29]. Reprinted with Springer's permission [29]. Copyright for Nature Medicine 2021.



Mammography Process Improvement Using Ai

In the upcoming years, DL appears prepared to move beyond its current function as a tool for mammography decision-support and become an independent reader of “ultra-normal” mammograms. In the United States, screening mammograms are conducted on over 20 million 22 women year, and over 99 percent of them are perfectly normal. There might be considerable cost savings and effects on workflow if an independent AI reader approved even a small portion of these studies without consulting a radiologist. This has been the subject of several studies [41–43], with the findings indicating that AI could be able to exclude up to 20% of the mammograms with the lowest chance of cancer without missing malignancies. Larger studies are required to confirm these encouraging results. Prior to clinical use, regulatory, medical-legal, and ethical concerns of standalone AI should be further considered.

Calcification

The ACR BI-RADS vocabulary is typically used to categorise calcifications, a frequent mammography finding, as worrisome, probably benign, or benign [36]. To enhance the classification process and prevent pointless biopsies, DL tools are being developed because more than half of calcifications that are categorised as worrisome have benign pathology [37]. Although the quantity of the data sets is limited, several researchers have shown improvements in diagnostic accuracy using DL algorithms. However, more extensive validation studies are required [38–40].

Deep Learning For Determining Breast Cancer Risk

Aimingtoimprovebreastcancerscreeningprocedures, DL has been applied in one of the most significant AI-for-medical-imaging advances to date. Currently, to evaluate if a woman is at high risk of developing breast cancer, which necessitates further screening using contrast-enhanced MRI in addition to the standard-of-care yearly screening mammography, traditional risk assessment models like the Tyrer-Cuzick model are utilised. Yala et al. and others have created DL models that outperform the Tyrer-Cuzick model using mammograms10,44,45 (or MR images12) and that have been externally evaluated using sizable and varied data sets from the US, EU, and Asia **(Figure 3)** [10]. The use of one commercial AI technology and one internal academic tool to predict future breast cancerrisk based on mammography pictures will be evaluated in the prospective study Screen Trust MRI, NCT04832594, which will improve the triage of women to further screening with breast MRI. Manley et al46 went a step further and showed that chemoprevention can reduce risk and their DL breast cancer risk score instrument is customizable. Additionally, DL tools have been created to automate the evaluation of mammographic breast density, and they have been used in radiology clinics, both academic and commercial [47,48].

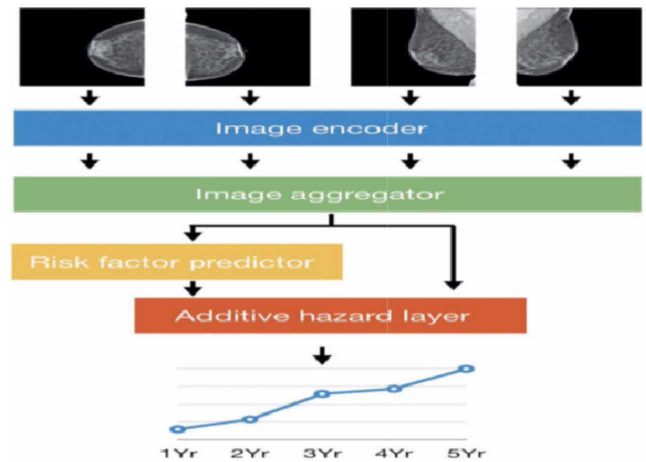


Figure 3 shows a schematic representation of the DL model for predicting breast cancer risk. 10 Four typical images of a single mammography are the model input. For all mammography views, the image encoder and image aggregator together generate a merged single vector. The DL model incorporates common clinical data (such as age and family history), and if any of these clinical variables are not accessible, a risk factor predictor module is utilised to fill in the gaps. The additive hazard layer, which incorporates imaging and clinical data, then forecasts breast cancer risk over a five-year period. Reprinted with permission from Science Translational Medicine, The American Association for the Advancement of Science, © 2021. DL, deep learning.

Ultrasound

Breast ultrasonography can be used as a diagnostic tool in the evaluation of mammographic or clinical findings as well as a supplemental screening modality (where it enhances the cancer detection rate over mammography alone, particularly in women with thick breasts) [49]. Unfortunately, ultrasonography frequentlyshowspoorspecificityandresultsinpointless biopsies. High inter reader variability is another issue. 50 Breast ultrasound lesion segmentation, lesion detection, and lesion classification DL approaches have been developed for both automated and portable ultrasound in an effort to improve the diagnostic efficacy of ultrasound. Automated breast ultrasound generates thousands of images per patient exam, and so DL tools are particularly needed for lesion detection and to reduce interpretation time.51 DL-based segmentation methods are state of the art, outperforming conventional computerized methods [51–53]. DL has also been applied to lesion detection and classification. [54–62] with several reader studies reporting DL models that are equivalent or superior to radiologists [49,62,63], although in most of these studies, DL models were compared against general radiologists without subspecialty training in breast imaging, small data set sizes were used, and data were from a single institution.58,62 As such, more work is needed to demonstrate the generalizability of these models. As a prognostication tool, DL for breast ultrasonography has also been investigated. With AUCs up to 0.90, Zhou et al [58] and Zheng et al. [64] employed ultrasound pictures of primary breast cancers to make this prediction. Figure 4 shows how to use ultrasound pictures of primary breast cancer to predict axillary nodal metastases using DL.

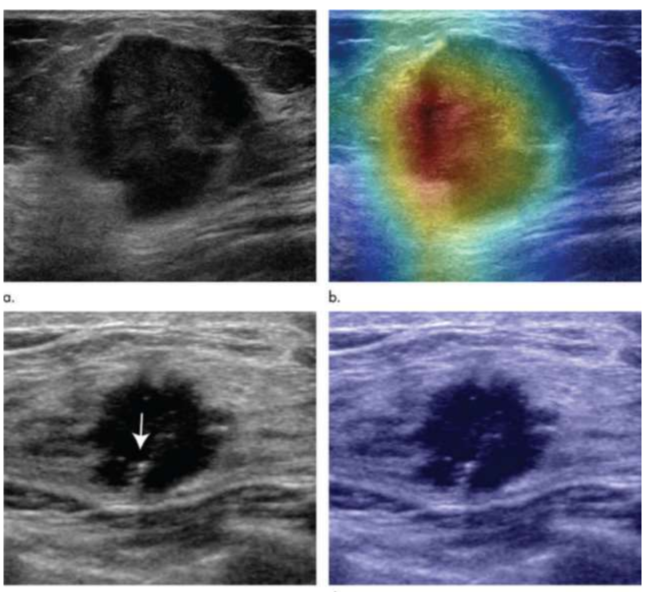


Figure 4 shows the ultrasound pictures of primary breast cancer in 2D and the DL-assisted prediction of clinically positive and negative lymph node metastases. 58 In this case, the use of DL allowed for the precise prediction of positive lymph node metastasis in 67-year-old females (a, b) and negative lymph node metastasis in 46-year-old females (c, d). Radiology, 58, reprinted with permission; 2020, Radiological Society of North America. Deep learning, or DL.

Imaging Of Magnetic Resonance

Breast MRI, the most sensitive technique for breast cancer diagnosis now on the market,65 is indispensable for screening high-risk women, determining the severity of the illness, gauging treatment effectiveness, and solving diagnostic conundrums. However, the cost and length of the exams frequently restrict their utilisation. High-resolution dynamic contrast-enhanced MRI is an information-rich imaging technique with many imaging sequences (such as T1W, T2W, DWI, and dynamic pre- and post-contrast imaging) reflecting various features of the underlying pathophysiology (e.g. water content, vascular permeability, etc.). This data-richness offers DL significant potential to learn new patterns that reveal novel associations between imaging and illness, offering up new paths for personalised treatment in addition to automating straightforward breast MR interpretation tasks. DL has so far been used in the segmentation of breast MR images, lesion identification, risk assessment, and therapy response. 66

Lesion Detection, Segmentation, And Classification

For 3D segmentation of breast MRI images, including segmentation of the whole breast, fibro glandular tissue (FGT), 69, 70 and mass lesions, 71, 72 DL is currently regarded as the most advanced technique (see Supplementary Material 1). Several organisations have used DL to identify and categorise lesions on breast MRIs73-81 (see Supplementary Material 1 for details). A 4D breast MRI dataset's magnitude makes en masse model training computationally challenging. Therefore, image pre-processing pipelines that extract therapeutically important spatial and temporal information are the foundation of breast MRI DL models. The most common (and simplest) method enables the use of common 2D CNN architectures for model training by converting a 4D data set into a 2D maximum intensity projection (MIP) of the subtraction picture (post-contrast minus pre-contrast) [73]. Various strategies have been tried out by other parties, such as: I employing a "MIP" of CNN uses 3D lesion ROIs, not whole pictures, in its features [73,74]. (ii), thus lowering the necessary data size and permitting the adoption of a 3D CNN, [76] (iii) using multi parametric data (such as T2, DWI), [76-78] and (iv) combining classical machine learning approaches with DL feature extraction discovering classifiers. In actuality, all breast MRI DL publications are constrained by the tiny data set size. the greatest studies to yet only including a few thousand breast cancer MRI scans Given the various sequences and the variances in protocol settings and naming standards, breast MRI tests are also notoriously difficult to curate.

Treatment Effectiveness And Risk Assessment

After intravenous contrast delivery, the background parenchymal enhancement (BPE) is a qualitative indicator of the augmentation of normal breast tissue. Similar to breast density, a radiologist's breast MRI report will contain information regarding BPE since it is a risk factor for breast cancer and to determine whether BPE limits the sensitivity for cancer detection [83]. When classifying BPE, radiologists exhibit high inter reader variability. BPE on breast MRI has been classified and segmented using DL, allowing for complete automation of this procedure.

Additionally,DLhasbeenusedtodirectlypredict5-year breast cancer risk from the breast MRI MIP picture, exceeding the gold standard Tyrer-Cuzick model in research similar to that done with mammography. Breast MRI data is particularly well-suited for more intricate DL-based prognostication because of its richness. Using pathology ground truth for the luminal A, luminal B, HER2+, and basal subtypes, DL using breast MRI images has been constructed to predict breast tumour molecular subtypes [86]. Using breast MRI data, other organisations have using DL to forecast the Oncotype Dx Recurrence Score. With good cross-validation accuracy, 89 DL has also been used to predict the axillary nodal status using breast MR images of the original tumour [90]. The use of DL methods to predict a patient's response to neo adjuvant chemotherapy is also a growing field of research. With AUCs of 0.81.93, the ground breaking I-SPY 2 study discovered that combinations of MRI characteristics can predict the pathologic treatment response. A number of teams are now combining pre- and post-neo adjuvant chemotherapy MRI scans with improved machine learning approaches to increase prediction ability. 13,14,91,94 Although a lot of this research is still in its early stages and only includes tiny data sets from a few universities, greater efforts in this field might eventually customise and improve cancer treatment.

Troubleshooting And Future Directions

Since 2016, the use of DL techniques in all facets of breast imaging has increased exponentially. Still, additional effort is required in a number of crucial areas. First, in order to determine if AI technologies will perform as predicted in clinical settings, sizable multi-institutional prospective studies managed by impartial third parties are required. A number of AI decision-support technologies have already received FDA approval, and retrospective and small reader studies demonstrate that AI mammography tools perform on par with or better than professional radiologists. 95 However, thorough assessment of these tools in a prospective environment is essential prior to responsible clinical usage. AI mammography methods have been retrospectively verified in a few significant multi-institutional external validation studies, while ultrasound and particularly MRI still require similar validation effort. The development of AI models for breast MRI has been promising, however it is significant to highlight that practically all published research employed modest data sets and were conducted by a single institution without external validation.

Since breast MRI techniques vary so much between institutions and even within the same institution over time, DL breast MRI projects can be particularly difficult. However, a breast MRI scan contains a multitude of information, and it continues to be a fruitful field of research with the potential to uncover new and better approaches to tailor the care of breast cancerpatientsinordertooptimisetherapeuticbenefit.
More technological effort is required to optimise AI tools for DBT in the field of mammography. It follows that DBT should perform better than AI-enhanced 2D mammography since radiologists discover more tumours and receive fewer call backs when using DBT than when using 2D mammography. But as of yet, this is not the case. Modern AI development for DBT is a technically difficult endeavour. DBT exam sizes are significantly bigger than in 2D mammography, resulting in significantly higher computing expenses during training that may result in technological constraints. Moreover, compared to 2D digital mammography, DBT picture post-processing is considerably less uniform among manufacturers, with notable differences in both acquisition approach (i.e. hardware) and reconstruction technique (i.e. software). Smaller DBT data sets are frequently made available. Nevertheless, a number of recent research have found positive findings and aim to shorten interpretation times. It is crucial to address the related ethical, medicolegal, and regulatory challenges as more AI technologies are created that have the potential for clinical translation. This is crucial for

standalone AI programmes that interpret breast imaging examinations on their own (i.e., in cases when no human radiologist examines the pictures) [81]. There are a lot of unsolved concerns on the ethical front. It could be crucial in scenarios where AI functions as a "black box," in which physicians act on the output of an AI tool without knowing how the algorithm came to its decision. When an AI technology misses a malignancy, who is responsible? How much should be under human control? An ethical issue with algorithms is prejudice. Constant care is required to manage possibly underrepresented minorities in the training data as AI models perform better on photos that match images in the training data set (e.g. racial groups, vendors, etc.). Additionally, more effort is required to increase the reliability of image normalisation methods so that DL models can more accurately generalise to data from institutions using various types of imaging gear or image post-processing software. Developing new legal mechanisms for thorough AI quality evaluation is also crucial. This might involve doing quality control tests on AI algorithms on a regular basis (much like imaging hardware does), as well as sometimes fine-tuning the algorithm to stop model performance from declining over time. Last but not least, one of the most startling findings in the literature to far is that using photos from many earlier time points does not result in better algorithm performance [30]. Although it is commonly established that having access to earlier mammograms significantly increases the diagnosis accuracy of breast imagers, the algorithms now in use cannot demonstrate equivalent gains. Clearly, there is room for technical advancement in this field.

CONCLUSION

In the upcoming years, the clinical environment of breast imaging is projected to undergo a significant change as DL technologies for breast imaging interpretation continue to advance quickly. Notably, DL mammography methods for detecting breast cancer and determining breast cancer risk exhibit performance atorabove humanlevels, andprospective studies are required to open the door to clinical use. New opportunities for disease prognostication and individualised treatments are made possible by more work on DL for breast imaging. To minimise algorithmic biases, stop AI "performance drift," and deal with the particular ethical, medico legal, and quality control challenges that DL algorithms offer, regulatory supervision is required when DL technologies are introduced into clinical practise.

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