



Artificial Intelligence - A Primer for Diagnosis and Interpretation of Breast Cancer

Dr. Anand Mohan Jha¹, Dr. Abikesh Prasada Kumar Mahapatra², Dr. John Abraham³ and Dr. Somenath Ghosh*

¹Post Graduate Department of Chemistry, M. L. S. M. College, Darbhanga (L. N. Mithila University, Darbhanga, Bihar)

²School of Pharmacy, OPJS University, Churu, Rajasthan, India

³Assistant Professor, Department of Family Medicine, St. Johns National Academy of Health Sciences, Bangalore, India- 560034

*Assistant Professor and Head, Rajendra Post-Graduate College, Jai Prakash University, Bihar, India

Abstract: Breast Cancer (BC) is a major universal health problem. Early detection and precise diagnosis are vital for enlightening outcomes. Artificial Intelligence (AI) technologies can potentially revolutionize the field of BC by providing quantitative representations of medical images to assist in segmentation, diagnosis, and prognosis. AI can improve image quality, detect and segment breast lesions, classify cancer and predict its behavior, and integrate data from multiple sources to predict clinical outcomes. It can lead to more personalized and effective treatment for BC patients. Challenges faced by AI in real-life solicitations include data curation, model interpretability, and run-through guidelines. However, the clinical implementation of AI is expected to deliver vital guidance for patient-tailored management. BC is a major global health problem; early detection and treatment are crucial for improving outcomes. Imaging detection is a key screening, diagnosis, and treatment effectiveness assessment tool. However, the irresistible number of images creates a heavy capacity for radiologists and delays reporting. AI has the potential to revolutionize BC imaging by improving efficiency and accuracy. AI can recognize, segment, and diagnose tumor lesions automatically and analyze tumor images on a molecular level. It could lead to more personalized treatment strategies. However, AI-assisted imaging diagnosis is still in its early stages of development, and more research is needed to validate its clinical effectiveness. Therefore, AI is a promising new technology that has the potential to progress the diagnosis and treatment of BC, and AI-assisted imaging diagnosis is a promising new technology for improving the early detection and diagnosis of BC. More research is needed to bring this technology to clinical practice.

Keywords: Breast Cancer, Artificial Intelligence, Digital mammography, Ultrasound, MRI for Breast Cancer, and AI in Breast Pathology.

*Corresponding Author

Dr. Somenath Ghosh , Post Graduate Department of Chemistry, M. L. S. M. College, Darbhanga (L. N. Mithila University, Darbhanga, Bihar)

Received On 7 December 2023

Revised On 19 December 2023

Accepted On 26 December 2023

Published On 5 January 2024

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation Dr. Anand Mohan Jha, Dr. Abikesh Prasada Kumar Mahapatra, Dr. John Abraham and Dr. Somenath Ghosh , Artificial Intelligence - A Primer for Diagnosis and Interpretation of Breast Cancer.(2024).Int. J. Trends in OncoSci.2(1), 27-36
<http://dx.doi.org/10.22376/ijtos.2024.2.1.27-36>

This article is under the CC BY- NC-ND Licence (<https://creativecommons.org/licenses/by-nc-nd/4.0>)

Copyright @ International Journal of trends in OncoScience, available at www.ijtos.com

Int. J. Trends in OncoSci., Volume2., No 1 (January) 2024, pp 27-36



1. INTRODUCTION

Breast Cancer (BC) accounts for over 2.4 million fresh cases (11.8%) and 0.7 million fatalities (6.8%) of all cancer cases globally. In a large number of nations, it is the most often detected cancer, and in 110 of those nations, it is the main factor in cancer-related death¹. Early identification and precise diagnosis of BC are crucial for improved results and to stop the spread of the illness. Age, genetics, genes, and environmental variables are only a few risk factors involved in the pathogenesis of the illness known as BC. BC also shows heterogeneity at the molecular and morphological levels². Several treatment strategies are required for people with various molecular subtypes to achieve the best results. Understanding the basis of BC is essential for accurate diagnosis and successful prognosis. Full-spectrum analyses can be addressed by non-invasive radiologic imaging, which provides promising options. Digital mammography (DM), digital breast tomosynthesis (DBTs), Ultrasound (US), magnetic resonance imaging (MRI), nuclear magnetic methods, or an amalgam of these, are often utilized modalities³. Early recognition and clinical staging of BC have both benefited greatly from the use of imaging detections. Nevertheless, several challenging concerns have recently gained more attention in clinical settings. On the other hand, radiologists have a significant burden because of the volume of imaging data that is created following the diagnosis of BC⁴. On the one hand, radiologists' ability to make accurate diagnoses is limited by pictures of inadequate quality or ambiguous characteristics. Demonstrating elusive or complicated disease symptoms may need both imaging and clinical data. Computer-aided diagnosis (CAD) suggests operative computerized lesion segmentation, picture identification, and diagnosis, possibly lowering radiologists' labor and increasing diagnostic precision⁵. The therapeutic relevance of CAD in BC has greatly increased due to the advancements in CAD, which have led to the development of more adaptable and versatile analyses, particularly image-based AI approaches. A dependable CAD methodology with advanced computer technology is necessary to enhance and assure the precision of diagnosis, which directly influences the assessment's accuracy⁶. The prompt detection of BC and the fall in death rates among individuals have been significantly helped by advancements in medical imaging modalities and technology. Current rapid developments in radioactive substances and deep learning technologies, as well as high-performance techniques for data analysis and AI technologies, have exponentially increased the creation of new AI-based models of breast images that address a wide range of application areas. BC is a complicated and ever-changing progression, making cancer management a challenging journey with many obstacles along the way⁷. Advancements in medical imaging technology and progress toward a better understanding of BC's intricate biological and chemical nature have significantly influenced the substantial decrease in BC mortality. In this therapeutic pipeline, the process of deciding on each of these tasks is greatly influenced by medical imaging. To identify suspicious tumors, gauge the likelihood of malignancy, and assess the prognosis for cancer, radiologists traditionally use descriptive or partially quantitative material visually gleaned from medical pictures⁸. Information that is clinically significant might involve patterns of improvement, the existence or inability of necrosis or bleeding, the density and size of suspicious tumors, tumor border fringe speculation, or the position of the distrustful tumor. Making a final diagnosis requires analyzing and combining information visually observed from medical imaging,

which is difficult. Despite being the most widely used imaging modality for BC screening, mammography usually performs poorly because of its lower sensitivity. The idea of AI, which entails teaching computers to execute activities that ordinarily entail human intellect, such as decision-making, speech recognition, and language translation, has existed since the 1950s⁹. It works effectively for processing massive amounts of heterogeneous, unstructured data from different imaging modalities to create high-dimensional associations.

2. BREAST CANCER IMAGING MODALITIES

BC is evaluated using radiological and unhealthy images, which take into account intrinsic abnormality characteristics like location, size, and morphology, cancer risk factors like malignant or benign, stage, and molecular types, and survival outcomes like metastasis, treatment response, and recurrence¹⁰. The following summary of the most popular imaging modalities: Digital mammography (DM) is frequently used to check for BC. From the ages of 40 to 75, depending on the national/regional screening programs, screening is conducted every 1, 2, or 3 years. It has been demonstrated that routine breast DM substantially lowers cancer-related mortality¹¹⁻¹³. In DM, the breast is exposed to X-rays, and the radiations are collected by a digital X-ray detector and converted into a two-dimensional (2D) digital picture. Mammography loses its precision, sensitivity, and reliability when breast tissues just vertically separated from one another look overlaid. This is especially true for thick breasts. Breast screening uses two perspectives of each breast—the cranio-caudal (CC) view and the medio-lateral oblique (MLO) view—to address this problem¹⁴. It is done by reestablishing a pseudo-3D image from multiple predictions, each obtained while the X-ray source was situated at a different angle, which increases sensitivity and specificity. Breast US is suggested as a first-line assessment for young women during pregnancy or nursing and is viewed as a supplemental evaluation, particularly for women with thick breasts. Breast US imaging can increase the global rate of detection by 17% when compared with DM. Regardless of breast density, MRI offers the best sensitivity among the current modalities for the examination of the breast for the diagnosis of occult malignancies¹⁵. In high-risk individuals, breast MRI (also known as DCE-MRI) is increasingly seen as a complement to DM. The increased sensitivity can be attributable to improved tissue contrast from cancer cell-absorbing contrast agents like gadolinium and comprehensive information offered by different scanning sequences such as shape, size, and blood perfusion. However, breast MRI is unsuitable for universal screening because of its high cost, limited specificity, lengthy examination duration, and constrained tolerance. Diagnostic approaches in radiation therapy includes positron emission tomography (PET) and molecular breast imaging (MBI). Breast PET uses an instrument adjacent to the breast to assess the absorption of fluorine 18 (¹⁸F) fluorodeoxyglucose (FDG) to identify metabolically active cancer cells. They have demonstrated their capacity for axillary lymphatic node (ALN) identification, categorization, and distant staging in BC¹⁶.

3. ULTRASOUND

Another imaging method for detecting BC is breast ultrasonography. Because it is non-radioactive and simple to use, it is frequently employed in assisted percutaneous biopsy and BC diagnosis. Ultrasound is a better alternative to mammography for small, non-calcified occult lesions¹⁷. There

are several types of breast ultrasound, such as automated full-volume breast scan imaging, ultrasonography, ultrasound light scattering tomography, ultrasound elastography, etc., alongside traditional breast ultrasound. These ultrasound-based detections combine several ultrasound contrast agents, 3D imaging technology, and spectral analysis technology based on conventional ultrasound to satisfy various diagnostic needs like evaluating the texture of tumors, differentiating between benign and malignant tissue and displaying its connection with the surrounding tissues¹⁸. The success rate of ultrasonography in the detection of BC has significantly increased with the newest invention of ultrasound elastography, and the semi-quantitative evaluation of lesion arduousness provides an improved distinction between swelling benignity and malignancy. In order to determine the condition of axillary lymph node metastases in clinical T₁₂ cancer, ultrasound elastography, and breast ultrasound imaging characteristics can be combined¹⁹. The workflow of ultra-sonographers and the interpretation of films by ultrasound physicians both suffer from considerable subjective biases that affect operator-dependent imaging modality and comprehensive AI identification of ultrasound pictures. Ultrasound image classification with AI is less developed than CT and MRI because it relies more on exchanging deep learning models between AI researchers and ultrasound experts²⁰. It is one reason AI identification of ultrasound images lags behind CT and MRI. To address this challenge, Singh et al. proposed a new breast ultrasound classification method using a contextual information-aware, firmly adversarial learning framework²¹. This method can effectively segment breast ultrasound images and handle a variety of tumors with different sizes and shapes.

4. MRI FOR BREAST CANCER

Breast MRI is an exceptionally susceptible and reliable imaging technique for determining the stage of BC before surgery, and the amount of tissue has no bearing on how sensitive it is to tumor diagnosis²². When genes are altered in BCs with vascular infiltration, this can be used to predict the likelihood of tumor vascular infiltration events and to assess the response to chemotherapy. MRI can provide information about the biological function of tumors. Spectral imaging can identify tissue regions' chemical composition for subjective tumor diagnosis by detecting metabolites. According to reports, MRI may be used to diagnose BC in a variety of ways, such as pathologic complete response (PCR) forecasting BC following neo-adjuvant treatment²³. Contrast-Enhanced Magnetic Resonance Imaging (CE-MRI) may offer various structures, including tumor morphology, texture, hemodynamics, and pharmacokinetics²⁴. Dynamic characteristics are a distinctive identification benefit of MRI above the two prior imaging exams, as they can aid in recognizing and categorizing tumors by demonstrating hemodynamic structures of tumors that are entirely distinct from those of normal glands. The viability of using DL to recognize breast tumor lesion-containing slides in MRI images was proven by Winkler and colleagues. They implemented the DL technique interested in the images and archiving communication system (ACS) to enhance the clinical workflow of viewing breast MRIs so that radiologists could rapidly select the desired image rather than scanning the imaging stack²⁵.

5. NUCLEAR MEDICINE TECHNIQUES

¹⁸F-Fluorodeoxyglucose (FDG) is a nuclear medicine test used in some cases of BC²⁶. Diagnoses, staging, evaluation of

recurring metastases, phenotypic identification, prognosis, and evaluation of therapeutic response are all covered by PET/CT in the case of BC in FDG. When compared to extra imaging tests, PET has the benefit of providing staging data for the entire body in a single scan²⁷. Due to the higher glucose metabolic background of brain parenchyma, PET/CT is not suited for identifying small intracranial metastases, and given the high cost, additional research is required to determine whether this test is price-effective for identifying early stages of BC. The adoption of composite imaging of ¹⁸F FDG-PET/CT with MRI in BC is encouraged by the greater diagnostic accuracy of MRI compared to other imaging tests. PET/MRI offers a 90–99% sensitivity for identifying BC and is more effective in staging the disease than PET/CT²⁸. PET scans use a small amount of radioactive tracer to create images of the body's tissues and organs. The tracer is injected into the bloodstream and travels to different body parts, where tissues absorb. A PET scanner detects the radiation from the tracer and creates images showing how much the tracer is in different body parts. PET scans can be used to detect cancer, including breast cancer²⁹.

6. RADIOMICS IN BREAST CANCER

AI-powered high-throughput picture recognition features, filtering using techniques based on the chosen evaluation or prediction endpoint events, model development with the screened features of images, and model validation with internal and external datasets³⁰. Entropy, tumor vascularity, and heterogeneity are correlated, and this information may be used to distinguish between benign and malignant BCs, according to radiomics research employing breast MRI scans. The predictive molecular markers HER2, progesterin receptor, and estrogen receptor were among those whose levels and statuses could be more clearly distinguished using the model created in this study³¹. A nomograph was created using medical characteristics based on radiomic algorithms to forecast the possibility of axillary lymph node metastasis and complications in people with initial BC. Radiomics examination of MRI was also used to forecast axillary lymph node metastasis in BC. Despite this study being retrospective, it has a substantial degree of MRI scan heterogeneity and a little follow-up time, and its results offer important guidance aimed at the practice of MRI-based imaging radiomics in the detection of BC. To deliver more detailed and customized radiological and genetic features, radiogenomics performs the joint examination of radiomics and genomics³². As a result, precision healthcare and customized treatment are no longer restricted to genetic or proteomics research projects that rely on tissue or blood samples. By analyzing alterations at the cellular level of the illness, radiogenomics research can aid in the prediction and early identification of cancer. Due to the numerous aspects of genetic testing, for example, DNA organizing and RNA sequencing, alongside the various image characteristics produced by various imaging exams, there are several distinct arrangements for imaging genomics analysis. A further benefit of imaging genomics is the ability to resolve imaging data of the entire lesion, which is unavailable by perforation or biopsy owing to tumor heterogeneity. It allows for acquiring complete data at the molecular level of genes inside the application. The Finished genetic and medical biomarkers for adult cancer have been connected by the Cancer Genome Atlas effort³³.

7. AI TECHNIQUES

The present phase of BC combating and prevention efforts is secondary prevention, or improving screening for high-hazard groups. Initial detection is also a critical part of BC control measures. The most valuable use of AI in BC screening might be the effective detection of malignant lesions among the enormous volume of photos of healthy individuals, significantly lessening the labor of imaging doctors. The establishment of computer-aided detection/diagnostic (CADe/CADx) systems underpins the establishment of AI-assisted breast imaging diagnosis. CAD is a key type of ML that helps radiologists detect small tumor lesions that they would have missed by fusing math, statistics, processing of images, and computer analysis³⁴. Fortunately, its use in healthcare is constrained by the high biopsy and false positive rates (FPR) associated with CAD detection³⁵. Learning is carried out to improve the efficacy of CAD, which covers the duties of clinical data set gathering, neural network standardized data set interpreting, ML classification algorithm selection, and system-wide performance assessment. The visual input data is utilized as an example set³⁶ to create a model. Making a DL-based AI application tool for BC diagnosis requires establishing a DL algorithm that is dependable across users, devices, and modalities and amassing a sizeable training dataset of great breast inspection photographs. The ability to annotate manually depends on the expertise of the imaging professional, and the manually drawn lesions serve as guidelines for automated segmentation³⁷. On the other hand, small-volume lesions or those with masked characteristics might be challenging to differentiate from adjacent healthy breast tissue. In AI for BC, there are two main forms of ML: regulated

education and spontaneous learning. This type of education identifies natural groups or categories in unlabeled data, whereas supervised learning trains models that map characteristics to categories using labeled data. Support vector machine (SVM), random forest (RF), and k-nearest neighbor (kNN) are examples of representative algorithms that are often used for medical imaging problems involving classification and regression³⁸. These algorithms work fine uniformly with little training data. Deep neural networks with many more layers are used in deep learning (DL), a subclass of ANN-based machine learning, to model complicated functions and identify high-level characteristics in data. The primary benefit of DL is its capacity to automatically derive rich representative features from unprocessed data, allowing it to discover latent semantic information about tasks. DL models are also adaptable since they can handle massive amounts of unstructured and heterogeneous data, learning from multi-modal pictures, audio, and text. To produce high-quality pictures for the image creation task, the generator and discriminator of the generative adversarial network (GAN) are alternately trained with various loss terms³⁹. In this scenario, the generator generates false data to trick the discriminator, who then tries to distinguish between the true data and the false data produced by the generator. When the created data is no longer distinct, the creator is changed and constructed on input from the discriminator from the real data⁴⁰. There are several uses for AI in the field of breast cancer, including medication research, tumor screening, diagnosis, staging, and therapy (Fig. 01).



Fig: I - Artificial Intelligence in clinical settings

8. BREAST IMAGE AUGMENTATION

The quest for improved picture quality is crucial for the clinical detection of BC. As a result, much recent research has used AI techniques for picture augmentation, including enhancement, synthesis, and creation techniques⁴¹. Given the scarcity of training samples for medical imaging models, AI-established data augmentation is also required to develop strong models. The results of these studies on BC show a notable improvement in clinical diagnosis accuracy to a 5% gain that can be attributable to US-synthesized. elastography⁴². Decreasing acquisition time, denoising, and contrast enhancement are just a few of the approaches under the heading of "Image enhancement techniques" that try to increase the accuracy of medical pictures. Picture resolution is severely compromised to speed up the reconstruction

process and decrease acquisition time. Scholars used a GAN-based super-resolution network to produce high-resolution DCE-MRI of BC from low-resolution ones in order to tackle this problem, which may enable a more precise diagnosis with better picture quality⁴³. Physicians may make a correct diagnosis with improved visualization, which is made possible by AI-based breast image denoising. Numerous networks, encompassing DM, DBT, US, MRI, and HP, are being used with various modalities. Domain gaps brought on by various scanning processes or suppliers threaten the generalizability of AI models. In medical settings, combo-mode screening, which combines 2D DM and 3D DBT, has been demonstrated to boost the specificity of diagnosis⁴⁴. Dual X-ray exposure, however, raises the risk of radiation-induced BC. Creating DM from DBT scratch using generative networks is one potential remedy. Compared to conventional B-mode US, the latest BC

imaging technology, elastography-ultrasound (EUS), offers higher sensitivity to soft tissue and tumor depth information. To offer data regarding tissue enhancement, DCE-MRI collects a sequence of pictures both before and after the injection of a contrast agent⁴⁵. Researchers used GAN-based models to create post-contrast pictures from pre-contrast images to limit the adverse effects of contrast agents, which achieved tissue enhancement and enhanced the diagnostic workflow for BC. A considerable quantity of training data is necessary to create an AI model effectively. Various dynamic networks have been used to add synthetic breast pictures to training samples to solve this problem, broadening the data dispersion and enhancing the capacity for extrapolation of the network⁴⁶. Due to their ability to produce a variety of realistic pictures, GANs, and their variations have shown to be very useful for data enrichment.

9. MEDICAL IMAGING CHARACTERISTICS AND TUMOR ENVIRONMENT RELATIONSHIPS

Discovering the connections between medical image characteristics and the tumor microenvironment is a key goal of BC research in the field of medical imaging in order to have more accurately forecast clinical outcomes. Since hand-crafting a collection of characteristics is necessary for typical CAD schemes, it is crucial to comprehend what descriptors correspond with radio mic-based genetic biomarkers particular to cancer⁴⁷. A hypoxic environment develops as tumors spread and enlarge due to a reduction in the amount of oxygen that is readily accessible due to increased demand. The tumor will go into an angiogenic state, which modifies the microvasculature in response to the newly hypoxic condition. In order to effectively supply the tumor with oxygen and nutrients, the tumor will activate angiogenic growth factors such as vascular-endothelial-growth-factor (ViEGF) and fibroblast-growth-factors (FiGF)⁴⁸. Most malignancies are characterized by nonhierarchical, immature, and extremely absorbent capillaries distinct from normal vasculature. This phenomenon is known as angiogenesis. Even while enhanced angiogenesis and high MVD have been linked as biomarkers of poor prognosis, MVD measurement is vulnerable to inter- and intra-reader variability, making it an unreliable and non-standardized diagnostic⁴⁹. The creation of a rapid, non-invasive biomarker that can distinguish between severely immature angiogenic and normal vasculature has been a popular area of study over the past ten years. The tumor microenvironment may be found and described using DCE-MRI, a non-invasive technique. Many research studies have shown the connection between DCE-MRI and tumor angiogenesis by correlating quantitative and semi-quantitative DCE-MRI-based kinetic characteristics with MVD. The contrast agent's escape from the tumor is shown by the peak signal enhancement ratio (peak SER) and washout fraction (WF), two semi-quantitative measures taken from the contrast augmentation curve. As fast washout will occur with immature and leaky vessels, these measures strongly correspond to a highly angiogenic state^{50,51}. It takes a pharmacokinetic analysis with high time resolution and frequently inadequate spatial resolution to gather quantitative information from DCE-MRI. Clinical DCE-MRI scans favor spatial firmness over temporal firmness, making it challenging to do a completely quantitative analysis. It may be possible to distinguish between conventionally rounded benign tumors and spiculated malignant tumors using shape-based characteristics. Mammography compression makes it challenging to obtain these features. Additionally, features may

be retrieved to quantify the tumor speculations, which will be very useful for identifying malignant BCs.

10. BREAST LESION DETECTION AND SEGMENTATION

A skilled radiologist reviews screening mammograms, but the interpretation procedure could be more varied, drawn out, and prone to mistakes. The intricacy of mammography and the number of tests each radiologist does might cause them to misinterpret the true diagnosis⁵². Overuse of mammograms for BC screening has been studied for a long time, which strongly encouraged the development of other medical imaging methods such as tumor detection, localization, segmentation, and classification. Additionally, locating and segmenting the suspicious area of the tumor is a difficult and time-consuming job⁵³. It is clear that a tumor may exist in any part of the breast, and a single breast may have several lesion occurrences, making it challenging to identify multiple worrisome areas and categorize them appropriately. Because it is possible for benign and malignancies to coexist on the same breast and overlap, this issue needs to be dealt with very precise⁵⁴. It calls for them to be independently classified and contoured (segmented) for the radiologists' benefit. Heterogeneous lesions seen in a single mammogram are not identified and segregated independently in current computer-aided diagnostic models. Consequently, multiple detection and segmentation of breast lesions might aid radiologists in making a precise diagnosis⁵⁵. AI-powered lesion detection techniques are highly accurate and effective and may be divided into two categories. The first uses bounding boxes on lesions, such as micro-calcification clusters, provided by detection networks like RCNN, Fast-RCNN, and Yolov4. Nevertheless, such identification techniques must be more accurate and prone to making false-positive predictions⁵⁶. The second method produces ROI contours that define lesion borders using classification networks with class activation maps (CAMs). A revolutionary, completely automated technique is presented to make lesion diagnosis easier in dynamic contrast-enhanced magnetic resonance mammography (DCE-MRM). The approach uses a cellular neural network to identify breast areas from pre-contrast pictures, creates normalized maximum 12*12 intensity-time ratio (nMITR) maps, and uses 3D template matching with three layers of cells to find lesions⁵⁷. A radiologist uses DCE-MRM to discover and assess lesions based on their morphology, enhancement dynamics, or both after initially identifying enhancing areas and marking a region of interest (ROI). The radiologist cannot visually review all of the captured and generated. Pictures for MRM: this assessment procedure takes time and requires skill⁵⁸. The last diagnosis may need more accuracy and specificity due to the absence of a very minor feature. As a result, computerized methods that aid radiologists in choosing options are being developed. These methods often use intensity differences between pre-and post-contrast pictures to extract characteristics⁵⁹.

11. AI IN BREAST PATHOLOGY

Breast pathologists frequently have several interpretations to do because of difficult diagnoses and time-consuming, repetitive activities, including calculating biomarker levels and assessing lymph node metastases. These activities need time and effort and are prone to inter-observer variability⁶⁰. Recent AI-integrated digital pathology processing improvements have shown intriguing solutions to these problems. Accurate

categorization of BC is essential for treatment choices, and histopathologic diagnosis of BC forms the cornerstone of therapeutic therapy. Recently, scientists created ML/DL algorithms to recognize and categorize breast tumors. To facilitate the multi-classification of BC histopathologic kinds, such as ductal carcinoma, lobular carcinoma, mucinous carcinoma, papillary carcinoma, etc., Han et al.¹⁴ ⁶¹ suggested a unique DL model. Economically accessible AI systems (algorithms) are accessible to identify/screen breast lesions in breast core biopsy samples. The GALEN Breast algorithm is one illustration. The algorithm is capable of screening the entirety of breast core needle biopsy WSIs to generate heat maps for various breast lesions, such as invasive carcinoma (ductal and lobular), in situ carcinoma (ductal and lobular), and atypical hyperplasia (ductal and lobular), as well as benign findings, such as sclerosing adenosis, fat necrosis, etc. Since lymph node metastases are significantly connected with prognosis, accurate identification of axillary lymph node metastasis in BC patients is essential for their clinical care. Assessment of lymph node metastases requires a lot of time and effort. While locating macro-metastasis is simple, finding single tumor cells or micro-metastasis may be more difficult. According to recent studies, AI algorithms can increase the precision and effectiveness of lymph node evaluation. TILs in the tumor's microenvironment are linked to improved therapeutic response and overall survival in BC, particularly triple-negative BC and HER2 breast carcinoma⁶². TILs are becoming more and more common as a BC biomarker. Manual evaluation of TILs is personal, has high inter-observer fluctuation, and has subpar repeatability. Seeking to produce more precise and repeatable outcomes, AI algorithms have been created to analyze TILs in light of the increased adoption of digital pathology. The degree of lymphocytic infiltrate in HER2 breast carcinoma was consequently detected and graded in one study using WSIs⁶³. The outcomes demonstrated that the architectural set of characteristics effectively differentiated samples with high and low lymphocytic infiltrate the amount with a precision of classification greater than ninety percent⁶⁴. Adopting AI algorithms in breast pathology requires taking into account several important issues. The initial one is the volume and caliber of training data used to create the AI algorithm. File formats for WSIs, scanner quality, and glass slide quality differ significantly in terms of stained intensity, coverslip size, tissue size, folded tissue, air bubbles, and so on⁶⁵. To create thorough ML/DL models, manual selection of WSIs with artifact-free and appropriate quality must be employed during algorithm training. Second, before their adoption for usage in therapeutic settings, AI algorithms must be validated⁶⁶. Except for some breast biomarker quantification AI algorithms, many of the above AI algorithms are still experimental. Recent research has shown that AI algorithms may be successfully validated, and institutions have begun to use such AI algorithms for clinical practice. Thirdly, if using AI algorithms to automate normal pathology practice, a digital pathology workflow (digital sign-out) is always recommended or required⁶⁷. Many organizations worldwide have adopted whole-sheet imaging technology, but only a few pathology labs have a fully digital pathology process.

12. PROGNOSIS

To guarantee the best prognosis, the appropriate therapy should be administered to the appropriate people based on the threat assessment for BC. Considering the intricate nature of the etiology and pathophysiology of BC, a patient-tailored

treatment ought to consider a variety of layers of info from radiologic data, pathologic data, genome, epigenome, transcriptome, proteome, and more⁶⁸. Integrating this multi-omics data with AI technology has been investigated to help with accurate cancer prognostic prediction. When extracting useful characteristics that might be used in therapeutic situations, AI is particularly good at identifying complicated picture patterns, creating quantitative feature representations, and integrating multi-omics data streams. The process of decoding radiologic pictures into quantitative characteristics is called AI-based radiomics⁶⁹. AI-based radiogenomics tries to link the genotype and tumor imaging phenotype. The likelihood of recurrence is decreased by forecasting lymph node (for example, ALN) metastasis, which gives helpful data for treatment planning. In multi-modal imaging, AI shows potential for determining ALN metastases. To anticipate ALN and SLN metastases in multi-modal imaging, AI-based radiomics models seem promising⁷⁰. DCE-MRI was employed in various investigations because of its multi-parametric ability to represent tumor heterogeneity. For instance, Yu et al. retrospectively gathered people from four institutions who had DCE-MRI images done before surgery. With radiomics and DL approaches recording characteristics for long-term monitoring of tumors, AI is being employed to expect treatment response (i.e., immunotherapy and targeted flash therapy)⁷¹. Radioactivity powered by AI for therapy DCE-MRI performed well when combined with clinical data to predict PCR, improving accuracy. AI-based radiomics analysis, in turn, is widely used to estimate BC patients' overall survival (OS), disease-specific survival (DSS), and disease-free survival (DFS)⁷².

13. CHALLENGES AND PROSPECTS

BC is still a very serious illness, and more common. The probable mode to lower the disease's death rate is still early identification during regular screening checks. The effectiveness of the present breast screening program, which includes both sensitivity and specificity, must be enhanced. It is growing for more challenging and time-consuming for medical professionals to process all of the data that is accessible, make an accurate diagnosis and develop an effective, individualized course of action as a result of the growth in the number of breast imaging techniques and the abundance of clinical, pathological, and genetic information. AI-based models for forecasting now have considerably broader implications in BC research than only the typical work of identifying and classifying worrisome breast lesions in CAD schemes⁷³. The use of AI in treating BC has opened the way for the development of customized medicine since cancer detection and diagnosis are now driven by quantitative data about specific individuals rather than general qualitative indicators⁷⁴. Even though much research has been done on creating and testing innovative AI-based models in the lab, only some of these studies or prototypes have made their way to clinical practice. It might be related to several difficulties or problems. Due to inevitable bias and model overfitting, training a model with a short dataset frequently has low universality and poor performance. The presence of widespread and first-class picture collections for various application activities is thus a significant barrier. Despite several breast image databases, including Digital Database for Screening Mammography, INbreast, MIAS, and BCDR, being accessible to the public, these repositories mostly feature straightforward instances and lack complex cases, significantly limiting their variety and heterogeneity⁷⁵. Many of the records mentioned in earlier

studies must be updated (e.g., Digital Database for Screening Mammography and MIAS used digitized screen-film-based mammograms), lacking biopsy-approved ground-truth medical images, or both. Efficient and reliable segmentation of breast lesions from the variable backdrop tissue is still challenging, whether lesion segmentation is carried out automatically or semi-automatically using a preliminary seed. AI-based software, such as (CAD) systems, has been created to expand the breadth of AI treatments in the clinical process⁷⁶. Nevertheless, the manually created features-based convolutional CADs have many false-positive discoveries. It is encouraging to note that DL-based systems have been created with performance superior to traditional CADs and even on par with highly skilled radiologists⁷⁷. Large amounts of high-quality data pose a significant obstacle to creating automated healthcare solutions since human tagging is expensive and inefficient. Establishing open-source image libraries through cross-institutional data exchange is a successful technique to expand the amount of data. However, there is substantial picture heterogeneity due to various institutions, scanners, acquisition protocols, and post-processing algorithms. Data augmentation and DL technologies may improve data quality and quantity; via supervised learning, they can reduce the need for data annotation; and through transfer learning, they can use models already trained on huge datasets. Most AI algorithms are designed retrospectively and absent prospective validation, which is essential to guarantee the model's resilience and generalizability.

17 REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-49. doi: 10.3322/caac.21660, PMID 33538338.
2. Sharma A, Hooda N, Sharma R, Gupta NR. A review of environmental pollutants as breast cancer risk factor. *AIP Conf Proc*. 2023 Feb 3;2558(1). doi: 10.1063/5.0120685.
3. Irmici G, Della Pepa G, D'Ascoli E, De Berardinis C, Giambersio E, Rabiolo L et al. Exploring the potential of artificial intelligence in breast ultrasound. *Crit Rev Oncog™ in Oncogenesis*. 2023. doi: 10.1615/CritRevOncog.2023048873.
4. Mello-Thoms C, Mello CAB. Clinical applications of artificial intelligence in radiology. *Br J Radiol*. 2023 Apr;96(1150):20221031. doi: 10.1259/bjr.20221031, PMID 37099398.
5. Silva HECD, Santos GNM, Leite AF, Mesquita CRM, Figueiredo PTS, Stefani CM et al. The use of artificial intelligence tools in cancer detection compared to the traditional diagnostic imaging methods: an overview of the systematic reviews. *PLOS ONE*. 2023 Oct 5;18(10):e0292063. doi: 10.1371/journal.pone.0292063, PMID 37796946.
6. Villa-Camacho JC, Baikpour M, Chou SS. Artificial intelligence for breast US. *J Breast Imaging*. 2023 Jan 1;5(1):11-20. doi: 10.1093/jbi/wbac077.
7. Bellini D, Milan M, Bordin A, Rizzi R, Rengo M, Vicini S et al. A focus on the synergy of radiomics and RNA sequencing in breast cancer. *Int J Mol Sci*. 2023 Apr

14. CONCLUSION

AI-based imaging analysis is crucial for BC prognosis, image augmentation, diagnosis, and segmentation. Despite challenges, AI can integrate multi-data streams into diagnostic systems, accelerating patient-tailored management. Integrating AI algorithms into clinical workflows can improve patient outcomes and reduce radiologists' workloads. AI-assisted BC diagnosis offers a promising model, but supplementary optimization and authentication in clinical tribunals are needed. A breakthrough in AI-specific databases and health insurance could accelerate its development. AI techniques may be included in the current clinical workflow to facilitate full-stack evaluation of BC and improve patient results while lessening radiologists' workloads.

15 AUTHORS CONTRIBUTION STATEMENT

Dr. Anand Mohan Jha conceived the study and was responsible for the overall direction, analysis, and planning. Dr. Abikesh Prasada Kumar Mahapatra Scarried out the implementation. Dr. John Abraham Mahmood took the lead in writing the manuscript. Gurman Kaur provided critical feedback, reviewed, and helped in the final corrections of the manuscript.

16 CONFLICT OF INTEREST

Conflict of interest declared none.

- 13;24(8):7214. doi: 10.3390/ijms24087214, PMID 37108377.
8. Kjær EKR, Vase CB, Rossing M, Ahlborn LB, Hjalgrim LL. Detection of circulating tumor-derived material in peripheral blood of pediatric sarcoma patients: A systematic review. *Transl Oncol*. 2023 Aug 1;34:101690. doi: 10.1016/j.tranon.2023.101690, PMID 37201250.
9. Shah N. Artificial intelligence in pharma industry-A review. *Asian J Pharm (AJP)*. 2023 Jun 15;17(2).
10. Moghbel M, Ooi CY, Ismail N, Hau YW, Memari N. A review of breast boundary and pectoral muscle segmentation methods in computer-aided detection/diagnosis of breast mammography. *Artif Intell Rev*. 2020;53(3):1873-918. doi: 10.1007/s10462-019-09721-8.
11. Riggio AI, Varley KE, Welm AL. The lingering mysteries of metastatic recurrence in breast cancer. *Br J Cancer*. 2021;124(1):13-26. doi: 10.1038/s41416-020-01161-4, PMID 33239679.
12. Tabar L, Yen MF, Vitak B, Chen HH, Smith RA, Duffy SW. Mammography service screening and mortality in breast cancer patients: 20-year follow-up before and after introduction of screening. *Lancet*. 2003;361(9367):1405-10. doi: 10.1016/S0140-6736(03)13143-1, PMID 12727392.
13. Feig S. Cost-effectiveness of mammography, MRI, and ultrasonography for breast cancer screening. *Radiol Clin North Am*. 2010;48(5):879-91. doi: 10.1016/j.rcl.2010.06.002, PMID 20868891.
14. Zhang J, Wu J, Zhou XS, Shi F, Shen D. Recent advancements in artificial intelligence for breast cancer: image augmentation, segmentation, diagnosis, and

- prognosis approaches. *Semin Cancer Biol.* 2023 Sep 12;96:11-25. doi: 10.1016/j.semcancer.2023.09.001, PMID 37704183.
15. Zhi H, Ou B, Luo BM, Feng X, Wen YL, Yang HY. Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions. *J Ultrasound Med.* 2007;26(6):807-15. doi: 10.7863/jum.2007.26.6.807, PMID 17526612.
16. van Geel JJJ, de Vries EFJ, van Kruchten M, Hospers GAP, Glaudemans AWJM, Schröder CP. Molecular imaging as biomarker for treatment response and outcome in breast cancer. *Ther Adv Med Oncol.* 2023 May;15:17588359231170738. doi: 10.1177/17588359231170738, PMID 37223262.
17. Dahan M, Cortet M, Lafon C, Padilla F. Combination of focused ultrasound, immunotherapy, and chemotherapy: new perspectives in breast cancer therapy. *J Ultrasound Med.* 2023 Feb;42(3):559-73. doi: 10.1002/jum.16053, PMID 35869903.
18. Jacob G, Jose I, Sujatha S. Breast cancer detection: A comparative review on passive and active thermography. *Infrared Phys Technol.* 2023 Sep 30;134:104932. doi: 10.1016/j.infrared.2023.104932.
19. Windsor GO, Bai H, Lourenco AP, Jiao Z. Application of artificial intelligence in predicting lymph node metastasis in breast cancer. *Front Radiol.* 2023 Feb 20;3:928639. doi: 10.3389/fradi.2023.928639, PMID 37492388.
20. Simmons L, Feng L, Fatemi-Ardekani A, Noseworthy M. Breast cancer calcifications and implications in medical imaging. *Crit RevTM in Biomedical Engineering.*
21. Singh VK, Abdel-Nasser M, Akram F, Rashwan HA, Sarker MMK, Pandey N et al. Breast tumor segmentation in ultrasound images using contextual-information-aware deep adversarial learning framework. *Expert Syst Appl.* 2020;162:113870. doi: 10.1016/j.eswa.2020.113870.
22. Muzahir S, Ulaner GA, Schuster DM. Evaluation of treatment response in patients with breast cancer. *PET Clin.* 2023 Jun 6;18(4):517-30. doi: 10.1016/j.cpet.2023.04.007, PMID 37291018.
23. Lo Gullo RL, Marcus E, Huayanay J, Eskreis-Winkler S, Thakur S, Teuwen J et al. Artificial intelligence-enhanced breast MRI: applications in breast cancer primary treatment response assessment and prediction. *Invest Radiol.* 2023 Jul 27:10-97. doi: 10.1097/RLI.0000000000001010, PMID 37493391.
24. Zheng D, He X, Jing J. Overview of artificial intelligence in breast cancer medical imaging. *J Clin Med.* 2023 Jan 4;12(2):419. doi: 10.3390/jcm12020419, PMID 36675348.
25. Thakur N, Kumar P, Kumar A. A systematic review of machine and deep learning techniques for the identification and classification of breast cancer through medical image modalities. *Multimedia Tool Appl.* 2023 Sep 28:1-94. doi: 10.1007/s11042-023-16634-w.
26. Pontico M, Conte M, Petronella F, Frantellizzi V, De Feo MS, Di Luzio D et al. 18F-fluorodeoxyglucose (18F-FDG) functionalized gold nanoparticles (GNPs) for plasmonic photothermal ablation of cancer: a review. *Pharmaceutics.* 2023 Jan 18;15(2):319. doi: 10.3390/pharmaceutics15020319, PMID 36839641.
27. Treglia G, Albano D, Dondi F, Bertagna F, Gheysens O. A role of FDG PET/CT for Response Assessment in Large Vessel Disease? *Nucl Med.* 2023 Jan 1 (Vol. 53, No. 1, pp. 78-85);53(1):78-85. doi: 10.1053/j.semnuclmed.2022.08.002, PMID 36075772.
28. Di Micco R, Santurro L, Gasparri ML, Zuber V, Cisternino G, Baleri S; et al. PET/MRI for Staging the Axilla in Breast Cancer: Current Evidence and the Rationale for SNB vs. PET/MRI.
29. Sutherland DEK, Azad AA, Murphy DG, Eapen RS, Kostos L, Hofman MS. Role of FDG PET/CT in management of patients with prostate cancer. *Semin Nucl Med.* 2023 Jul 1. doi: 10.1053/j.semnuclmed.2023.06.005, PMID 37400321.
30. Moore NS, McWilliam A, Aneja S. Bladder cancer radiation oncology of the future: prognostic modelling, radiomics, and treatment planning with artificial intelligence. *Radiat Oncol.* 2023 Jan 1 (Vol. 33, No. 1, pp. 70-75);33(1):70-5. doi: 10.1016/j.semradonc.2022.10.009, PMID 36517196.
31. Corredor G, Bharadwaj S, Pathak T, Viswanathan VS, Toro P, Madabhushi A. A review of AI-based radiomics and computational pathology approaches in triple-negative breast cancer: current applications and perspectives. *Clin Breast Cancer.* 2023 Jun 21. doi: 10.1016/j.clbc.2023.06.004.
32. Romeo V, Moy L, Pinker K. AI-enhanced PET and MR imaging for patients with breast cancer. *PET Clin.* 2023 Jun 17;18(4):567-75. doi: 10.1016/j.cpet.2023.05.002.
33. Srivastava R. Applications of artificial intelligence multiomics in precision oncology. *J Cancer Res Clin Oncol.* 2023 Jan;149(1):503-10. doi: 10.1007/s00432-022-04161-4, PMID 35796775.
34. Mohammadi S, Livani MA. A Review of CAD systems for Breast Mass Detection in Mammography Based on Deep Learning.
35. Din M, Agarwal S, Grzeda M, Wood DA, Modat M, Booth TC. Detection of cerebral aneurysms using artificial intelligence: a systematic review and meta-analysis. *J NeuroIntervent Surg.* 2023 Mar 1;15(3):262-71. doi: 10.1136/jnis-2022-019456, PMID 36375834.
36. Hinton GE, Osindero S, Teh YW. A fast learning algorithm for deep belief nets. *Neural Comput.* 2006;18(7):1527-54. doi: 10.1162/neco.2006.18.7.1527, PMID 16764513.
37. Lotter W, Diab AR, Haslam B, Kim JG, Grisot G, Wu E; et al. Robust breast cancer detection in mammography and digital breast tomosynthesis using an annotation-efficient deep learning approach. *Nat.*
38. Mhaske H, Patil M, Thote J, Shendage A, Tallapalli R. A review on melanoma cancer detection using artificial intelligence. *IJRASET;11(2):1335-9.* doi: 10.22214/ijraset.2023.49231.
39. Morrison TM, Stitzel JD, Levine SM Modeling and Simulation in Biomedical Engineering: Regulatory Science and Innovation for Advancing Public Health. *Ann Biomed Eng.* 2023;51(1):1-5. doi: 10.1007/s10439-022-03116-7. PMID 36562847.
40. Hong TS, Tomé WVA, Harari PM. Heterogeneity in head and neck IMRT target design and clinical practice. *Radiother Oncol.* 2012;103(1):92-8. doi: 10.1016/j.radonc.2012.02.010, PMID 22405806.
41. Poplack SP, Park EY, Ferrara KW. Optical breast imaging: a review of physical principles, technologies, and clinical applications. *J Breast Imaging.* 2023 Sep 1;5(5):520-37. doi: 10.1093/jbi/wbad057.
42. Yao Z, Luo T, Dong Y, Jia X, Deng Y, Wu G, et al. Virtual elastography ultrasound via generative adversarial network for breast cancer diagnosis. *Nat*

- Commun. 2023;14(1):788. doi: 10.1038/s41467-023-36102-1, PMID 36774357.
43. Jiang G, He Z, Zhou Y, Wei J, Xu Y, Zeng H et al. Multi-scale cascaded networks for the synthesis of a mammogram to decrease intensity distortion and increase model-based perceptual similarity. *Med Phys.* 2023;50(2):837-53. doi: 10.1002/mp.16007, PMID 36196045.
44. Jiang G, Wei J, Xu Y, He Z, Zeng H, Wu J et al. Synthesis of mammogram from digital breast tomosynthesis using deep convolutional neural network with gradient guided cGANs. *IEEE Trans Med Imaging.* 2021;40(8):2080-91. doi: 10.1109/TMI.2021.3071544, PMID 33826513.
45. Avtanski D, Hadzi-Petrushev N, Josifovska S, Mladenov M, Reddy V. Emerging technologies in adipose tissue research. *Adipocyte.* 2023 Dec 31;12(1):2248673. doi: 10.1080/21623945.2023.2248673, PMID 37599422.
46. Oza P, Sharma P, Patel S, Adedoyin F, Bruno A. Image augmentation techniques for mammogram analysis. *J Imaging.* 2022;8(5). doi: 10.3390/jimaging8050141, PMID 35621905.
47. Rizzo S, Botta F, Raimondi S, Origgi D, Fanciullo C, Morganti AG, et al. Radiomics: the facts and the challenges of image analysis. *Eur Radiol Exp.* 2018;2(1):36. doi: 10.1186/s41747-018-0068-z, PMID 30426318.
48. Madu CO, Wang S, Madu CO, Lu Y. Angiogenesis in breast cancer progression, diagnosis, and treatment. *J Cancer.* 2020;11(15):4474-94. doi: 10.7150/jca.44313, PMID 32489466.
49. Schneider BP, Miller KD. Angiogenesis of breast cancer. *J Clin Oncol.* 2005;23(8):1782-90. doi: 10.1200/JCO.2005.12.017, PMID 15755986.
50. Kim SH, Lee HS, Kang BJ, Song BJ, Kim HB, Lee H, et al. Dynamic contrast enhanced MRI perfusion parameters as imaging biomarkers of angiogenesis. *PLOS ONE.* 2016;11(12):e0168632. doi: 10.1371/journal.pone.0168632, PMID 28036342.
51. Mori N, Abe H, Mugikura S, Takasawa C, Sato S, Miyashita M, et al. Ultrafast dynamic contrast-enhanced breast MRI: kinetic curve assessment using empirical mathematical model validated with histological microvessel density. *Acad Radiol* (2019) 26(7):e141–e9. doi: 10.1016/j.acra.2018.08.016
52. Makhtar M, Yang L, Neagu D, Ridley M. Optimisation of classifier ensemble for predictive toxicology applications *Proc 14th Int. Conf. Model Simulation, UKSim 2012.* Vol. 2012; 2012. p. 236-41. doi: 10.1109/UKSim.2012.41.
53. Yang D, Wang Y, Jiao Z. Asymmetry analysis with sparse autoencoder in mammography; 2016. doi: 10.1145/3007669.3007712.
54. Ribli D, Horváth A, Unger Z, Pollner P, Csabai I. Detecting and classifying lesions in mammograms with Deep Learning. *Sci Rep.* 2018;8(1):4165. doi: 10.1038/s41598-018-22437-z, PMID 29545529.
55. Yurdusev AA, Adem K, Hekim M. Detection and classification of microcalcifications in mammograms images using difference filter and Yolov4 deep learning model. *Biomed Signal Process Control.* 2023;80:104360. doi: 10.1016/j.bspc.2022.104360.
56. Mota AM, Clarkson MJ, Almeida P, Matela N. Detection of microcalcifications in digital breast tomosynthesis using faster R-CNN and 3D volume rendering. In: *Proceedings of the 15th international joint conference on biomedical engineering system and technologies (Bioimaging).* Vol. 2; 2022. p. 80-9. doi: 10.5220/0010938800003123.
57. Li Y, He Z, Ma X, Zeng W, Liu J, Xu W, et al. Architectural distortion detection based on superior–inferior directional context and anatomic prior knowledge in digital breast tomosynthesis. *Med Phys.* 2022;49(6):3749-68. doi: 10.1002/mp.15631, PMID 35338787.
58. Li Y, He Z, Pan J, Zeng W, Liu J, Zeng Z, et al. Atypical architectural distortion detection in digital breast tomosynthesis: a computer-aided detection model with adaptive receptive field. *Phys Med Biol.* 2023;68(4). doi: 10.1088/1361-6560/acaba7, PMID 36595312.
59. Li Y, He Z, Ma X, Zeng W, Liu J, Xu W, et al. Computer-aided detection for architectural distortion: a comparison of digital breast tomosynthesis and digital mammography. *J Med Imaging.* 2022;12033:231-8. doi: 10.1117/12.2611287.
60. Han Z, Wei B, Zheng Y, Yin Y, Li K, Li S. Breast cancer multi-classification from histopathological images with structured deep learning model. *Sci Rep.* 2017;7(1):4172. doi: 10.1038/s41598-017-04075-z, PMID 28646155.
61. Busby D, Grauer R, Pandav K, Khosla A, Jain P, Menon M et al. Applications of artificial intelligence in prostate cancer histopathology. *Urol Oncol.* 2023 Jan 11. doi: 10.1016/j.urolonc.2022.12.002, PMID 36639335.
62. Tran J, Thaper A, Lopetegui-Lia N, Ali A. Locoregional recurrence in triple negative breast cancer: past, present, and future. *Expert Rev Anticancer Ther.* 2023 Oct 3(just-accepted);23(10):1085-93. doi: 10.1080/14737140.2023.2262760, PMID 37750222.
63. Fatima GN, Fatma H, Saraf SK. Vaccines in breast cancer: challenges and breakthroughs. *Diagnostics (Basel).* 2023 Jun 26;13(13):2175. doi: 10.3390/diagnostics13132175, PMID 37443570.
64. Issa-Nummer Y, Darb-Esfahani S, Loibl S, Kunz G, Nekljudova V, Schrader I, et al. Prospective validation of immunological infiltrate for prediction of response to neoadjuvant chemotherapy in HER2-negative breast cancer—a substudy of the neoadjuvant GeparQuinto trial. *PLOS ONE.* 2013;8(12):e79775. doi: 10.1371/journal.pone.0079775, PMID 24312450.
65. Ono M, Tsuda H, Shimizu C, Yamamoto S, Shibata T, Yamamoto H, et al. Tumor-infiltrating lymphocytes are correlated with response to neoadjuvant chemotherapy in triple-negative breast cancer. *Breast Cancer Res Treat.* 2012;132(3):793-805. doi: 10.1007/s10549-011-1554-7, PMID 21562709.
66. Savas P, Teo ZL, Lefevre C, Flensburg C, Caramia F, Alsop K, et al. The subclonal architecture of metastatic breast cancer: results from a prospective community-based rapid autopsy program "Cascade". *PLOS Med.* 2016;13(12):e1002204. doi: 10.1371/journal.pmed.1002204, PMID 28027312.
67. Maley CC, Koelble K, Natrajan R, Aktipis A, Yuan Y. An ecological measure of immune-cancer colocalization as a prognostic factor for breast cancer. *Breast Cancer Res.* 2015;17(1):131. doi: 10.1186/s13058-015-0638-4, PMID 26395345.
68. Peck RW. The right dose for every patient: a key step for precision medicine. *Nat Rev Drug Discov.* 2016;15(3):145-6. doi: 10.1038/nrd.2015.22, PMID 26669674.

69. Aerts HJ, Velazquez ER, Leijenaar RT, Parmar C, Grossmann P, Carvalho S, et al. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. *Nat Commun.* 2014;5:4006. doi: 10.1038/ncomms5006, PMID 24892406.
70. Lambin P, Leijenaar RTH, Deist TM, Peerlings J, De Jong EEC, Van Timmeren J, et al. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol.* 2017;14(12):749-62. doi: 10.1038/nrclinonc.2017.141, PMID 28975929.
71. Polevoy GG, Kumar DS, Daripelli S, Prasanna M. Flash therapy for cancer: A potentially new radiotherapy methodology. *Cureus.* Oct 13, 2023;15(10):e46928. doi: 10.7759/cureus.46928.
72. Park H, Lim Y, Ko ES, Cho HH, Lee JE, Han BK et al. Radiomics signature on magnetic resonance imaging: association with disease-free survival in patients with invasive breast cancer. *Clin Cancer Res.* 2018;24(19):4705-14. doi: 10.1158/1078-0432.CCR-17-3783, PMID 29914892.
73. Lehman CD, Wellman RD, Buist DS, Kerlikowske K, Tosteson AN, Miglioretti DL, et al. Diagnostic accuracy of digital screening mammography with and without computer-aided detection. *JAMA Intern Med.* 2015;175(11):1828-37. doi: 10.1001/jamainternmed.2015.5231, PMID 26414882.
74. Giger ML, Karssemeijer N, Schnabel JA. Breast image analysis for risk assessment, detection, diagnosis, and treatment of cancer. *Annu Rev Biomed Eng.* 2013;15:327-57. doi: 10.1146/annurev-bioeng-071812-152416, PMID 23683087.
75. Antropova N, Huynh BQ, Giger ML. A deep feature fusion methodology for breast cancer diagnosis demonstrated on three imaging modality datasets. *Med Phys.* 2017;44(10):5162-71. doi: 10.1002/mp.12453, PMID 28681390.
76. Conant EF, Toledano AY, Periaswamy S, Fotin SV, Go J, Boatsman JE et al. Improving Accuracy and Efficiency with Concurrent Use of Artificial Intelligence for Digital Breast Tomosynthesis. *Radiol Artif Intell.* 2019;1(4):e180096. doi: 10.1148/ryai.2019180096, PMID 32076660.
77. Maghsoudi OH, Gastounioti A, Scott C, Pantalone L, Wu F-F, Cohen EA et al. Deep-LIBRA: an artificialintelligence method for robust quantification of breast density with independent.