NARRATIVE REVIEW

Transforming breast cancer care: harnessing the power of artificial intelligence and imaging for predicting pathological complete response. a narrative review

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Abstract

This narrative review explores the transformative potential of Artificial Intelligence (AI) and advanced imaging techniques in predicting Pathological Complete Response (pCR) in Breast Cancer (BC) patients undergoing Neo-Adjuvant Chemotherapy (NACT). Summarizing recent research findings underscores the significant strides made in the accurate assessment of pCR using AI, including deep learning and radiomics. Such AI-driven models offer promise in optimizing clinical decisions, personalizing treatment strategies, and potentially reducing the burden of unnecessary treatments, thereby improving patient outcomes. Furthermore, the review acknowledges the potential of AI to address healthcare disparities in Low- and Middle-Income Countries (LMICs), where accessible and scalable AI solutions may enhance BC management. Collaboration and international efforts are essential to fully unlock the potential of AI in BC care, offering hope for a more equitable and effective approach to treatment worldwide.

Keywords: Artificial Intelligence, Learning, Breast Neoplasms, Healthcare Disparities, Neoadjuvant Therapy, Radiomics, Neoadjuvant Therapy, Pathological Response, Magnetic Resonance Imaging

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Introduction

Breast cancer (BC) stands as the most common type of carcinoma among women on a global scale, with more than 90% of the individuals being staged between II to III at the time of diagnosis.[1,2] In 2020 alone, BC resulted in 685000 deaths worldwide.[3] In Asian nations like India and Pakistan, the incidence of BC is highest, according to reports, 178,388 new cases of BC were diagnosed in Pakistan in 2020.[4,5] In Pakistan, 1 in 9 women have developed BC at some point in their lives.[6]

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Historically, post-surgery patients when diagnosed with Locally Advanced Breast Cancer (LABC) typically underwent chemotherapy and radiation therapy. Neo-adjuvant chemotherapy (NACT) is a type of oncological treatment that shrinks and downstages the tumour and prevents the invasion of extra-glandular tissues. This, in turn, facilitates a more conservative surgical strategy.[7,8] An increasing number of patients are receiving NACT over the last few years, particularly in patients with some specific disease molecular subtypes like Triple Negative Breast Cancer (TNBC) and Human Epidermal Growth-Factor Receptors-2 (HER-2) positive tumours, as there is verifiable proof of better survival and effectiveness.[9-11]

The primary goal of NACT is to diminish the tumour size with resultant downstaging of the tumour and the attainment of Pathologic Complete Response (pCR), this implies the absence of any remaining invasive local disease and the lack of metastasis in axillary lymph nodes following NACT, denoted as ypT0N0/ypTisN0.[12] This permits for the possibility of Breast Conservation Surgery (BCS) in women who previously needed a mastectomy, as well as less comprehensive options for BCS. In addition, it removes the necessity for axillary dissection of lymph nodes in a subgroup of patients, thereby sparing them from the enduring complications of accompanying lymphoedema.[7,13] According to previous research studies, in patients with BC, pCR can be utilized as a short-term objective for longer survival.[14,15] However, 50–70% of NACT-treated individuals were reported to be unable to attain pCR.[16,17]

The ability to identify early responders and predict pCR to NACT is a clinical imperative. Identifying those most likely to benefit from NACT not only optimises treatment but also paves the way for omitting definitive surgery in select cases, thereby minimizing long-term morbidity.18 To date, a reliable, non-invasive method to evaluate response early in the NACT course remains lacking, presenting a substantial clinical gap.[18]

Breast cancer can frequently be characterized by imaging studies including Magnetic Resonance Imaging (MRI), mammography, and ultrasound. Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) gives valuable dynamic vascular, physiological, and anatomical information about the lesion by taking sequential images after intravenous contrast administration.[18] Radiological complete response determined by DCE-MRI has been demonstrated to forecast pCR with good sensitivity and specificity.[19] Although DCE-MRI is most often employed for the analysis of pCR, other pulse sequences including T2-Weighted sequences and Diffusion-Weighted sequences can also be utilized for the evaluation of pCR. Patients who achieve pCR are reported to experience better survival as compared to non-pCR patients, suggesting that response to treatment is a good predictor of prognosis.[19]

Early prediction (before commencement) of NACT effects in terms of pCR is an increasingly popular subject in current clinical studies because Identifying patients who will respond effectively to NACT early in the process is crucial for improving and adjusting the treatment regimen throughout the course of therapy, optimizing expenditures, and sparing these individuals from potentially inefficient or hazardous chemotherapy treatments or surgical interventions.[20-22]

The primary objective of this narrative review is to comprehensively examine the role of Artificial-Intelligence (AI), including Machine-Learning (ML), Deep-Learning (DL) and Convolutional Neural Network (CNN) in assessing pCR in BC patients after NACT. By conducting this review, we aim to provide a detailed understanding of the current state of AI in assessing pCR after NACT in BC and to shed light on its potential to shape future research, decision making, and the comprehensive management of patients with BC. Ultimately, our objective is to contribute to the advancement of BC care by harnessing the power of AI in optimizing treatment strategies and the patient outcomes.

Materials and Methods

To gather pertinent studies and literature, a systematic search was performed by querying electronic databases such as “Medline”, “PubMed”, “Web of Science”, “Scopus”, and “Google Scholar”. The search strategy incorporated a blend of keywords and Medical Subject Headings (MeSH) terms associated with breast cancer, neoadjuvant chemotherapy, pathological complete response, artificial intelligence, deep learning, convolutional neural networks, machine learning and radiomics. The search was not limited by publication date, and the latest articles available up to the knowledge cutoff date in October 2023 were included.

Inclusion Criteria

• Studies investigating the use of AI in predicting pCR in BC patients after NACT.
• Articles focussing on imaging techniques, including Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI), mammography, and ultrasound for assessing response to NACT.
• Research articles and clinical studies that have undergone peer review and have been published in reputable journals.
• Studies accessible in the English language.
• Relevance to the objectives of this narrative review.

Exclusion Criteria

Studies were excluded if they did not pertain to the subject of interest or if they were duplicates of previously identified publications. Additionally, articles not accessible through our electronic database search or not available in the English language were excluded.

The selected articles were critically reviewed, and relevant data were extracted. The information retrieved included: Study details, Patient characteristics, Imaging techniques, AI methods and models and Outcomes. The findings from the selected studies were synthesized to offer an overview of the present state of AI-assisted imaging techniques for predicting pCR in BC patients undergoing NACT. The methodological quality of the selected studies was scrutinized to assess the thoroughness and credibility of the research. This narrative review does not involve any primary research or human subjects; hence, no ethical approval or consent was required. Moreover, it's important to acknowledge that the quality and accessibility of data within the chosen articles may differ, potentially impacting the extent of analysis and the generalizability of the findings The findings of this narrative review will be presented and discussed in the main body of the review, with an emphasis on the role of AI in assessing pCR in BC patients following NACT and its potential impact on clinical decision-making and patient outcomes.

Discussion

Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) assumes a crucial role in BC research, facilitating the transformation of medical images into data with high-dimensional characteristics, and creating radiomic signatures that encompass diverse quantitative imaging characteristics, including shape, texture, and dynamics.[23,24] Various ML techniques, such as supervised, self-supervised, and unsupervised learning, are employed to analyse radiomics data.[24] Supervised learning relies on labelled datasets, self-supervised learning generates labels from unlabelled data, and unsupervised learning identifies underlying patterns without labels. Notably, DL

Table-1: Studies addressing AI-Driven Approaches for Predicting Pathological Complete Response (pCR) in Breast Cancer Patients.

Author	Study Type	Research Goal	AI Approach	Study Findings	Conclusions
Yu-Hong Qu, et al.[27]	Retrospective study	Create a deep learning algorithm to predict pCR following NACT in BC.	Utilized Deep Learning Network with pre-NACT and post-NACT MRI data.	Achieved an AUC of 0.970 by combining pre-NACT and post-NACT data.	Combining pre-NACT and post-NACT MRI data enhances pCR prediction.
Qin Li, et al. [28]	Retrospective study	Evaluate radiomics based on multiphase CE-MRI for early pCR prediction in HER-2 positive invasive BC.	Employed Machine Learning Classifiers based on CE1 and CEm radiomic features.	Attained an AUC of 0.84 for the CEM-based model; 76%-84% accuracy in various groups.	Multiphase CE-MRI may provide non-invasive early pCR prediction in HER-2 positive BC.
Elizabeth J. Sutton, et al.[29]	Retrospective study	Develop and validate a radiomics classifier for classifying BC pCR on MRI post-NAC before surgery.	Employed Radiomics Analysis and Recursive Feature Elimination Random Forest.	Achieved AUROC of 0.72 for model 1 and 0.80 for model 2 in pCR prediction.	Radiomics-based classifier accurately predicts pCR on MRI post-NAC.
Raffaella Massafra, et al. [30]	Retrospective study	Develop an AI method using deep learning to predict pCR using DCE-MRI at different protocols.	Utilized Deep Learning with sagittal and axial DCE-MRI data.	Obtained accuracies of 84.4% and 77.3%, with AUC values of 80.3% and 78.0% on independent tests.	AI method is robust for pCR prediction across various DCE-MRI protocols.
Chenchen Li, et al [31]	Retrospective study	Construct a preoperative predictive model based on tumoral and peritumoral volumes of multiparametric MRI.	Involved in Radiomic Feature Extraction and Support Vector Machine modelling.	Achieved AUCs of 0.96 for tumoral VOI, and 0.97 for peritumoral VOI in the training cohort.	Multiparametric MRI radiomics model effectively predicts pCR in BC.
Panli Li, et al.[32]	Retrospective study	Identify radiomic predictors from 18F-FDG PET/CT scans for predicting pCR in BC patients before NAC.	Employed Machine Learning Models with PET/CT radiomic features.	Attained an AUC of 0.844 on the training set and 0.767 on the independent validation set.	PET/CT radiomic predictors combined with age can effectively predict pCR after NACT.

Abbreviations: Neo-Adjuvant Chemotherapy: NACT, AUC: Area Under the Curve, pCR: Pathological Complete Response, HER-2: Human Epithelial Growth Factor Receptor-2, MRI: Magnetic Resonance Imaging, CE-MRI: Contrast-Enhanced Magnetic Resonance Imaging, CE1: 1st Post-contrast CE-MRI Phase, CEm: Multi-phase Contrast-Enhanced MRI, SVM: Support Vector Machine, FDG PET/CT: 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography.

techniques, particularly CNNs, have emerged as powerful tools, surpassing traditional machine learning methods.[24,25] Incorporating clinical variables, including demographics, molecular subtypes, and laboratory results, can enhance the prediction of pCR, which can be profoundly influenced by molecular subtypes.[26] Epigenetic factors and the evolving molecular state during therapy can also impact pCR, making MRI valuable for monitoring changes over time. The integration of DL holds promises for precise pCR prediction, guiding BC treatment, given its capability to handle extensive and complex datasets, both imaging and non-imaging.[26] Table-1 displays the included studies.

In a retrospective study by Qin Li et al. (2021),[28] focussed on patients with HER-2 positive BC, multiphase DCE-MRI was employed to predict pCR to NACT. They analysed 127 patients who underwent multiphase DCE-MRI both before and during NACT and subsequent surgical resection. ML models were developed using 1st phase and multiphase DCE-MRI data, utilizing radiomic features. Of 23 classifiers, logistic regression based on the 1st phase achieved an Area Under Curve (AUC) of 0.69 with a maximum accuracy of 68.5%, while linear Support Vector Machine (SVM) based on multiphase DCE-MRI attained an AUC of 0.84, outperforming the logistic regression model. The linear SVM model showed an accuracy of 84% in the mass enhancement group and 76% in the non-mass enhancement group. The study concluded that ML models utilizing multiphase DCE-MRI can effectively predict pCR to NACT in HER-2 positive BC, offering valuable insights into tumour heterogeneity and early treatment response.[28] Similarly correlating pCR with molecular subtypes, Elizabeth J. Sutton et al. (2020) conducted a retrospective study on 278 BC cases using DCE-MRI after-NACT. The dataset was split into 80% training sets and 20% testing sets. The radiomics-based ML models showed promising results in classifying pCR. Model 1, using radiomics alone, achieved an Area Under Receiver Operator Curve (AUROC) of 0.83 in the test set. Model 2, combining radiomics with molecular subtype, attained an AUROC of 0.78 in the test set. Model 3, which used only radiomics characteristics and no MRI intensity features, also performed well, indicating the potential of radiomics for predicting post-NACT pCR.[29] Like the above mentioned studies, Raffaella Massafra et al.[30] (2022) conducted a study evaluating the robustness of a DL model using sagittal and axial breast DCE-MRI images to predict pCR post-NACT. They used two datasets: a public dataset with 151 patients (40 pCR, 109 non-pCR) and a private dataset with 74 patients (22 pCR, 52 non-pCR). The patients in both datasets had DCE-MRI exams before NACT. A pre-trained CNN was employed to extract features. The study revealed significant correlations between pCR and histological variables, including Estrogen Receptors (ER), Progesterone Receptors (PR), HER-2, Ki-67 levels, grading, and clinical data. The SVM classifier achieved an accuracy of 80.3% and 78.0% for the public and private datasets, respectively, when clinical characteristics were added to the features concentration technique (F-merged).[30]

In a multicentre study by Li Chenchen et al.,[31] a ML model based on DCE-MRI radiomics was developed for preoperative prediction of pCR in patients with invasive non-metastatic ductal carcinoma undergoing NACT. The study included 448 patients diagnosed and treated with BC between November 2011 and July 2019 at the two hospitals. All patients had preoperative DCE-MRI and postoperative surgical histopathology data available. The tumour regions were segmented, and radiomic features were extracted from Contrast-Enhanced T1-weighted imaging; T1+C, Diffusion-Weighted Imaging with quantitative measurement; DWI-ADC, and the T2-Weighted fat-suppression Imaging; T2WI. A total of 863 quantitative characteristics were analysed, leading to highly accurate prediction models. The top 20-30 significant features in every MRI film sequence within two distinct Volumes of Interest were used to build prediction models. The tumour + peritumoral Interest Volumes multiparametric MRI radiomics model showed the most accurate prediction, achieving AUCs of 0.98 and 0.92 in the training set and validation set cohorts, respectively. In the training/validation set cohorts, the combined-sequence tumour Interest Volumes model had AUCs of 0.96 and 0.89, while the peritumoral Interest Volume model had AUCs of 0.97 and 0.78. In the training set cohort, the pCR rate was 10.5%, while in the validation set cohort, it was 18.5%. This study introduces a highly accurate model for predicting preoperative pCR in non-metastatic invasive ductal BC patients undergoing NACT, utilising both tumoural and peritumoural radiomic features extracted from preoperative MRI imaging's. [31]

In a retrospective study of 302 BC patients meeting strict inclusion criteria, which included LABC non-metastatic patients who underwent pre-NACT contrast-enhanced MRI examination within 7 days before NACT, post-NACT MRI examination within 3 days after completing NACT, and subsequently, these individuals underwent surgical resection. With available post-surgical histopathology results, a DL model which combined both before and after-NACT MRI data demonstrated significant potential for predicting pCR. The post-NACT model demonstrated an AUC of 0.968, whereas the combined model, incorporating both before and after-NACT data, showed an AUC of 0.970. The combined model's specificity was notably more, i.e., 100%, than the after-NACT model's (84.9%), and its positive predictive value was also superior (100% vs. 82.8%). Decision curve analysis revealed the overall benefits of deep learning across the risk threshold range (27). In another study by Panli Li et al. (32), a ML model was developed to predict pCR in patients with LABC using pre-NACT FDG PET/CT imaging. The study included 100 patients with confirmed non-metastatic BC who underwent PET/CT scans within 7 days before NACT and later had surgical excisions with post-surgical histopathology as the gold standard. The patients randomized to training set cohort (70) and a testing set cohort (30), with equal proportions of pCR cases in both cohorts. The primary endpoint was pCR. Radiomics features were extracted from PET/CT scans and analysed using various ML models. The predictive radiomics model, combining PET and CT features along with patient age, attained an AUC of 0.948 and accuracy of 0.857 in the training set. In the testing set, the model achieved an AUC of 0.73 and accuracy of 0.8. This study illustrates the efficacy of a model in forecasting pCR prior to NACT using radiomics PET/CT data from a sole pre-treatment scan and age of the patients.[32]

While the studies discussed above offer valuable perspectives on the potential of AI and imaging techniques for predicting pCR in BC patients undergoing NACT, it is essential to acknowledge certain limitations inherent to this body of literature. First and foremost, the retrospective nature of these studies introduces inherent bias and potential confounders. Prospective studies with larger, diverse patient cohorts are necessary to validate the clinical utility and generalizability of these AI models. Furthermore, variations in imaging protocols, AI models, and data preprocessing techniques among these studies may affect the consistency and comparability of the results. Standardization of these aspects is crucial to facilitate cross-study comparisons and clinical implementation. Finally, the use of different AI approaches, such as deep learning and radiomics, while promising, warrants more extensive validation and head-to-head comparisons to identify the most effective and robust methodologies. These limitations emphasise the need for ongoing research, collaboration, and standardisation in the field of AI-assisted BC management to maximise the benefits for patients and clinicians.

Future implications

The promising results from the integration of AI and imaging techniques for predicting pCR in BC patients undergoing NACT hold significant implications for the future of oncology. AI-based models have the potential to revolutionise clinical decision-making by enabling early identification of NACT responders, optimising treatment strategies, and reducing the morbidity associated with unnecessary chemotherapy and surgical interventions. Moreover, AI may assist in tailoring personalised treatment plans based on a patient's predicted response, ultimately improving overall outcomes and quality of life. With the ever-increasing volume of healthcare data and technological advancements, the role of AI in BC care is poised for continued growth, ushering in an era of precision medicine. Additionally, the implementation of AI-powered screening and diagnostic tools could help bridge healthcare disparities in LMICs. These countries often face challenges in accessing specialised healthcare services, including BC treatment. AI-driven solutions, which can be cost-effective and scalable, may help improve early detection, treatment planning, and patient outcomes in resource-constrained settings, thereby reducing the global burden of breast cancer. Collaborative efforts and international partnerships are essential to ensure that AI technologies are accessible and beneficial for LMICs, contributing to more equitable healthcare worldwide.

Conclusion

In conclusion, the integration of AI and advanced imaging techniques, such as DCE-MRI, has shown great promise in the prediction of pCR in BC patients undergoing NACT. These AI-driven models, including deep learning and radiomics-based approaches, have demonstrated their ability to accurately assess and predict pCR, ultimately guiding clinical decision-making and improving patient outcomes. Furthermore, in LMICs, AI applications hold the potential to address healthcare disparities and improve BC management by providing cost-effective and scalable solutions. Collaborative efforts are essential to harness the full potential of AI in BC care and extend its benefits to a global population.

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