Multimodal Data-Driven Intelligent Systems for Breast Cancer Prediction – A Review

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Abstract

Cancer is a manifestation of abnormal condition of the body's cells, characterized by rapid cell growth. Breast cancer occurs when breast cells proliferate and multiply uncontrollably. Early detection and diagnosis of breast cancer are proved to invariably reduce the mortality rate. Recent advancements in medical science namely Artificial Intelligence based prediction / diagnosis models are proved to be more reliable and promising in disease diagnosis and decision-making. This article comprehends on the reported research work related to breast cancer detection using multimodal data. The primary motivation behind the comprehensive literature review from existing literature provides the lack of conventional unimodal analysis evolved into multimodal frameworks, which this review aims to address. The exploration of literature confirms the viability of developing an efficient Intelligent System for Breast Cancer Detection, being trained on the Multimodal dataset.

Keywords: Breast cancer, convolutional neural networks, genomic data, multimodality

1. Introduction

Breast cancer has recently surpassed other cancers incidents and has emerged as the predominant cause of malignancy, especially among women [1]. Globally, about 10% of breast cancer is genetic or induced due to an inherited DNA mutation. But a recent study suggests that there is a higher probability of occurrence of genetically linked breast cancer among Indian women. Most of the inherited breast cancer cases are caused by the defective breast cancer genes namely, BRCA1, and BRCA2, where BRCA stands for breast cancer. The Lancet study [2] has radically changed the present perspectives of breast cancer as its molecular hallmarks are extensively characterised by a variety of biomarkers including, immunohistochemical markers, genomic markers, and immunomarkers. Now, the choice of treatment for breast cancer therapy indicates its complexity and effectiveness. This scenario demands scientific and systematic efforts to develop research strategies for accurate early diagnosis and classification of breast cancer, better than the existing methods. Early identification of breast cancer can help raise the chances of survival. With improvements in ML and DL, it is now easy to develop an automated and accurate Computer Aided Diagnosis (CAD) system to make the entire process of identifying a malignant tumor [3,4] more resource effective and saves a lot of precious time which can be used for effective treatment.

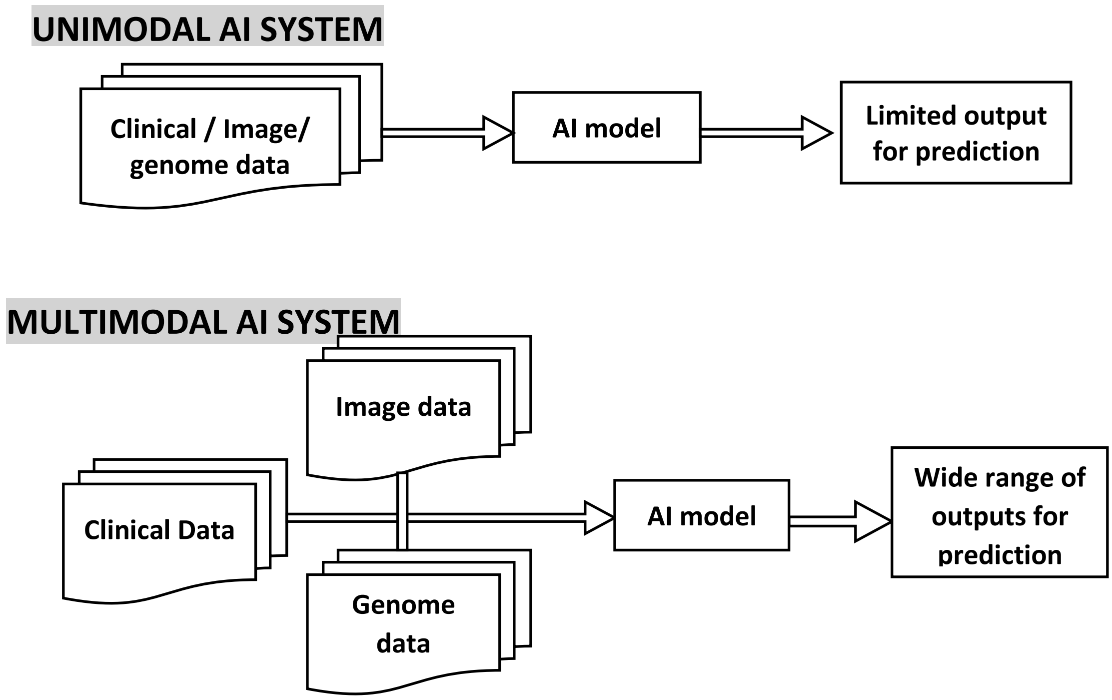

Fig 1. Unimodal and multimodal AI Systems

There are many research works based on unimodal data and multimodal data for breast cancer prognosis with the help of clinical data, imaging biomarkers, and with the identification of gene markers. However, traditional breast cancer prediction methods largely rely on unimodal data, which are inadequate to capture the full spectrum of breast cancer features. Unfortunately, traditional unimodality breast cancer prediction methods have proven to be insufficient in accurately diagnosing breast cancer. Due to their single-mode nature, these techniques often overlook important factors such as microcalcifications or architectural distortions that can be indicative of malignancy. As a result, unimodality breast cancer prediction is no longer considered an adequate way of diagnosing this disease. To improve accuracy and reduce medical errors, it is essential to develop a multi-modal approach for breast cancer prediction that combines different imaging modalities [5]. This will result in more accurate and reliable diagnosis of breast cancer. Figure 1 shows the unimodal and multimodal Artificial Intelligence (AI) systems [6]. Such research is expected to provide new directions in health care and pharmaceuticals towards personalized drug design, drug delivery, and to customize suitable therapeutic care.

2. Literature Review

Breast cancer is a devastating disease that continues to plague women across the globe. It has a high mortality rate and is particularly severe, especially in younger age groups. Recent studies have shown that the prevalence of breast cancer among younger age groups has exceeded the worldwide average. To further understand this deadly disease and improve its prognosis, researchers are using unimodal and multimodal data to aid in the prediction of breast cancer. This includes clinical data, imaging biomarkers, and the identification of gene markers. This review work provides the basis for the study provided by existing solutions of breast cancer predictions.

2.1. Reviews on Unimodal data

Unimodal dataset classification involves the use of data to make predictions about outcomes or classify specific types of data. Unimodal datasets, which consist of data from a single source can provide valuable insights into the development and progression of breast cancer. The use of unimodal datasets to predict breast cancer can be effective when the data source is highly informative.

Van't Veer *et. al.,* [7] used DNA microarray analysis on primary breast tumors from 117 patients and utilized a supervised classification method to recognize a 70-gene prognostic signature, and then, established a prognosis signature to identify the BRCA carriers. Poor signature results in invasion, metastasis, and angiogenesis, thus obtaining better performance, results in predicting disease outcomes better.

Yap *et. al.*, [8] used deep learning (DL) approaches for breast lesion detection from ultrasound images. They investigated the performance of LeNet, U-Net, and a pretrained AlexNet. They conducted their experiments on two custom datasets of 306 and 163 images termed dataset A and dataset B, respectively. Their pretrained AlexNet-based model achieved the best overall performance by achieving an F-measure of 0.91 and 0.89 on both datasets.

Antari et al., [9] suggested a Deep Learning integrated architecture capable of classification, segmentation, and detection for the classification of benign and malignant breast tumors. They used full resolution convolutional network (FrCN) for segmentation, a deep convolutional neural network (CNN) for classification, and You-Only-Look-Once (YOLO) for detection. They examined the INbreast database for digital X-ray mammograms. Their model has a mass detection accuracy of 98.96% and a dice score of 92.69% for mass segmentations. To augment the dataset, the authors applied rotation 8 times to synthetically increase the size of the dataset.

Al Najdawi et al., [10] have proposed a method to improve the performance of breast region segmentation using novel enhancement, segmentation, and classification approach. This method handled the mammogram in 4 orientations: RCC, LCC, RMLO, and LMLO. Histogram Equivalization and median filter is used for enhancement and removal of noise. Canny edge detection is applied for segmenting the breast region. The segmented Mass Region of interest (RoI) is processed for classification and analysis. The mass is classified among four classes: benign, probable benign-possible malignant, probable malignant-possible benign, and malignant, and the classification accuracy was 90.7%. 1,300 mammogram images were used from King Hussein Cancer Centre and Jordan Hospital.

Charan S. et al., [11] presented a new breast cancer detection method for mammograms using Convolutional Neural Networks (CNN). They used MIAS dataset, having 322 mammograms with 189 normal and 133 abnormal breasts. 70% of dataset was used as training samples and 30% as test samples. The parameters, Minimum Batch Size, Maximum Epoch, and Learning Rate were tuned for getting the optimum result for training. The accuracy on pre-processed images yielded better results than raw images, because the parameters were already learned and fixed. The overall accuracy of 65% was obtained on RoI datasets whereas it was 60% on raw datasets.

2.2. Reviews on Multimodal data

Multimodal datasets can be even more powerful when it comes to predicting breast cancer. By combining data from multiple sources, researchers can gain a better understanding of the disease and its progression. This can help to develop more effective treatments and improve outcomes for those affected by the disease. This has led to improved accuracy in diagnosing the disease, which can help reduce false positives or negatives. Additionally, multimodal datasets can be used to track breast cancer progression stages, allowing healthcare professionals to better inform patients on their individual risk factors and treatment options.

Sun D. *et. al.,* [12] proposed a breast cancer prediction method by integrating genomic data and pathological images. They worked on multiple kernel learning methods by comparing with different independent models trained on genomic, data and the results indicate that pathological images along with 10-fold cross-validation experiment could contribute to a remarkable prediction performance.

Gevaert *et. al.,* [13] developed Bayesian networks to integrate both clinical and those 70 gene information by three different strategies including full, decision or partial integration, and demonstrate that the use of clinical and microarray data has better or comparable performance than the methods with clinical or microarray data, respectively.

Sun D. *et. al.,* [14] improved the prognosis of breast cancer prediction by developing a multimodal deep neural network by integrating multidimensional data with the help of emerging deep learning methods. This method used Gene expression profile, copy number alteration profile, and clinical data which achieved better performance than the prediction methods with single dimensional data.

Khademi *et. al.,* [15] proposed a probabilistic graphical model (PGM) by integrating two independent models of microarray and clinical data for prognosis and diagnosis of breast cancer. They first applied Principal Component Analysis (PCA) to reduce the dimensionality of microarray data and construct a deep belief network to extract feature representation of the data. Then, the authors applied a structure learning algorithm to the clinical data and integrated both by using SoftMax nodes for obtaining prognosis of breast cancer.

Qian et al. 2021 [16] incorporated comparable modalities for breast cancer diagnosis, such as multimodal, multiview ultrasound imaging. Using the deep-learning framework, the model was constructed using view-level multimodal US images (that is, US B-mode, US colour Doppler, and US elastography images). This utilizes one-view multimodal US images as inputs for each prospective clinical test lesion, analyses the suspicious lesion from several viewpoints, and provides an overall malignancy likelihood. To predict malignancy risk probability and establish the Breast Imaging Reporting and Data System (BI-RADS) category, they used VGG19 with SENet, ResNet-50 with SENet and Inception-v3 with SENet and the performance of this model is tested with each combination of the bimodal and multimodal sets.

Binder *et. al.*, [17] proposed an explainable machine-learning-based method to ensure flexibly in identification and prediction of morphological as well as molecular tissue properties from histological breast cancer image data. The prediction is based on morphological feature training database containing manually annotated breast cell types in different data modalities with histological cancer images from TCGA in combination with molecular profiling data by providing heatmap visualizations.

Liu et al. [18] developed a deep learning prediction model for predicting the molecular subtype of breast cancer. They used gene modality data and image modality data for constructing multimodal fusion framework. For data pre-processing, PCA and image filtration methods are used for gene data and image data respectively. This framework used the Multimodal fusion of deep neural networks and convolutional neural networks for validating and achieving high accuracy levels.

Arya and Saha [19] suggested a multimodal based advanced deep learning models. They developed a sigmoid CNN for generating convoluted feature maps and random forest classifier for extracting stacked features for the prediction of breast cancer prognosis.

Table 1. Significant contributions on unimodal and multimodal breast cancer predictions

S. No.	Author(s)	AI Models used	Datasets Used	Significance of the Research	Evaluation Metrics
1.	Van't Veer *et. al.*,	Supervised classification and unsupervised cluster analysis	117 primary breast tumor patients	DNA microarray analysis to identify BRCA carriers	Oestrogen receptor (ER) signature group
2.	Yap *et. al.*,	LeNet, U-Net, and pretrained AlexNet.	US images 306 and 163 images	Breast lesion detection using ultrasound images	True Positive Fraction, False Positives per image, F-measure
3.	Antari et al.,	Full resolution Convolutional Network, Deep Convolutional Neural Network and You-Only-Look-Once (YOLO)	INbreast dataset	Classification, segmentation, and detection for the benign and malignant breast tumors	Accuracy and Dice score
4.	Charan S et al.,	Convolutional Neural Networks with Minimum batch size, Maximum epoch, and Learning rate	MIAS dataset	Breast Cancer Detection in Mammograms using Convolutional Neural Network	RoI accuracy and Raw image accuracy

S. No.	Author(s)	AI Models used	Datasets Used	Significance of the Research	Evaluation Metrics
5.	Sun D *et. al.,*	multiple kernel learning, 10-fold cross-validation	TCGA-BRCA dataset	Heterogeneous data for increasing performance than single dimensional data	Accuracy, specificity, precision sensitivity precision, Matthew's correlation coefficients, ROC curve
6.	Gevaert *et. al.,*	Markov blanket, Bayesian network	Integrated Tumor Transcriptome Array and Clinical data Analysis database	Integrate data sources and investigate the performance	RoC curve
7.	Sun D *et. al.,*	Deep Neural networks on single and multi-dimensional data	METABRIC dataset	Integrating multi-dimensional data for prognosis prediction	Accuracy, specificity, precision sensitivity precision, matthew's correlation coefficients, ROC curve
8.	Khademi *et. al.,*	Principal Component Analysis, deep belief network, structure learning algorithm with softMax	Netherlands Cancer Institute, METABRIC, Ljubljana Breast Cancer, Wisconsin Original, and Diagnostic Breast Cancer datasets	Integrating microarray and clinical data for breast cancer diagnosis	Accuracy
9.	Qian et al.,	VGG19 with SENet, ResNet-50 with SENet and Inception-v3 with SENet	10,815 multimodal breast-ultrasound images	Predicting the Multimodal multiview breast-ultrasound images	Area under the ROC curve
10.	Binder *et. al.,*	Morphomolecular correlation, clustering, and functional annotation	TCGA-BRCA Dataset	Predicting morphological and molecular tissue properties from histological breast cancer image data	Accuracy, heatmap visualization

S. No.	Author(s)	AI Models used	Datasets Used	Significance of the Research	Evaluation Metrics
11.	Liu et al.,	PCA, image filtration methods, deep neural nerworks and convolutional neural networks	TCGA-BRCA dataset	gene modality data and image modality data for constructing multimodal fusion framework	Accuracy
12.	Arya and Saha	Sigmoid CNN, random forest classifier	METABRIC and TCGA-BRCA datasets	Multimodal breast cancer prognosis prediction	Accuracy, specificity, precision sensitivity precision, matthew's correlation coefficients, ROC curve

Table 1 brief the related contributions on unimodal and multimodal breast cancer predictions. Research into breast cancer prediction has seen a shift in focus from unimodality to multimodality approaches. This research gap analysis will evaluate the effectiveness of the two methods and highlight potential areas for exploration and improvement. It is suggested for Deep learning models with multimodal data sources which are powerful because they can provide richer information than the former one. It can process on multiple sources of data that advantage over unimodal counterparts.

3. Conclusion

Breast cancer detection is one of the challenges for the oncologists. The ability to make accurate predictions about breast cancer through both unimodal and multimodal datasets is essential for health care professionals and researchers. Unimodal datasets can provide valuable insights into the development and progression of the disease, while multimodal datasets can provide a more complete picture that can lead to improved predictions. By combining data from multiple sources and using algorithms to analyze the data, it is possible to make more accurate predictions about breast cancer. The literature confirms that there are unique architectures for each data format. Deep learning models with multimodal data sources are powerful because they can provide more relevant information than the former one. It is apparent that the multiple modal data have an edge over the unimodal counterparts. Moreover, these models can also predict the probability of a patient developing breast cancer in the future.

References

[1] Mertz, S., Mayer, M., Paonessa, D., Papadopoulos, E., Alessandro, F., Peccatori, K. S., & Spence, D. (2016). Breast Cancer Center Survey: Cancer center management, support, and perception of mBC patient needs across 582 healthcare professionals.

[2] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32381-3/fulltext

[3] Bini, S. A. (2018). Artificial intelligence, machine learning, deep learning, and cognitive computing: what do these terms mean and how will they impact health care?. The Journal of arthroplasty, 33(8), 2358-2361.

[4] Karthik, S., Perumal, R. S., & Mouli, P. C. (2018). Breast cancer classification using deep neural networks. In Knowledge computing and its applications (pp. 227-241). Springer, Singapore.

[5] Stahlschmidt, S. R., Ulfenborg, B., & Synnergren, J. (2022). Multimodal deep learning for biomedical data fusion: a review. Briefings in Bioinformatics, 23(2), bbab569. https://doi.org/10.1093/bib/bbab569

[6] https://research.aimultiple.com/multimodal-learning/

[7] Van't Veer, L. J., Dai, H., Van De Vijver, M. J., He, Y. D., Hart, A. A., Mao, M., & Friend, S. H. (2002). Gene expression profiling predicts clinical outcome of breast cancer. nature, 415(6871), 530-536.

[8] Yap, M. H., Pons, G., Marti, J., Ganau, S., Sentis, M., Zwiggelaar, R., ... & Marti, R. (2017). Automated breast ultrasound lesions detection using convolutional neural networks. IEEE journal of biomedical and health informatics, 22(4), 1218-1226.

[9] Al-Antari, M. A., Al-Masni, M. A., Choi, M. T., Han, S. M., & Kim, T. S. (2018). A fully integrated computer-aided diagnosis system for digital X-ray mammograms via deep learning detection, segmentation, and classification. International journal of medical informatics, 117, 44-54.

[10] Al-Najdawi, N., Biltawi, M., & Tedmori, S. (2015). Mammogram image visual enhancement, mass segmentation and classification. Applied Soft Computing, 35, 175-185.

[11] Charan, S., Khan, M. J., & Khurshid, K. (2018, March). Breast cancer detection in mammograms using convolutional neural network. In 2018 International Conference on Computing, Mathematics and Engineering Technologies (iCoMET) (pp. 1-5). IEEE.

[12] Sun, D., Li, A., Tang, B., & Wang, M. (2018). Integrating genomic data and pathological images to effectively predict breast cancer clinical outcome. Computer methods and programs in biomedicine, 161, 45-53.

[13] Gevaert, O., Smet, F. D., Timmerman, D., Moreau, Y., & Moor, B. D. (2006). Predicting the prognosis of breast cancer by integrating clinical and microarray data with Bayesian networks. Bioinformatics, 22(14), e184-e190.

[14] Sun, D., Wang, M., & Li, A. (2018). A multimodal deep neural network for human breast cancer prognosis prediction by integrating multi-dimensional data. IEEE/ACM

transactions on computational biology and bioinformatics, 16(3), 841-850.

[15] Khademi, M., & Nedialkov, N. S. (2015). Probabilistic graphical models and deep belief networks for prognosis of breast cancer. In 2015 IEEE 14th International Conference on Machine Learning and Applications (ICMLA), IEEE, 7.27-732

[16] Qian, X., Pei, J., Zheng, H., Xie, X., Yan, L., Zhang, H., ... & Shung, K. K. (2021). Prospective assessment of breast cancer risk from multimodal multiview ultrasound images via clinically applicable deep learning. Nature biomedical engineering, 5(6), 522-532.

[17] Binder, A., Bockmayr, M., Hägele, M., Wienert, S., Heim, D., Hellweg, K.,& Klauschen, F. (2021). Morphological and molecular breast cancer profiling through explainable machine learning. Nature Machine Intelligence, 3(4), 355-366.

[18] Liu, T., Huang, J., Liao, T., Pu, R., Liu, S., & Peng, Y. (2022). A hybrid deep learning model for predicting molecular subtypes of human breast cancer using multimodal data. Irbm, 43(1), 62-74.

[19] Arya, N., & Saha, S. (2021). Multi-modal advanced deep learning architectures for breast cancer survival prediction. Knowledge-Based Systems, 221, 106965.