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An Advent Approach for Diagnosis and Prediction of Breast Cancer by Single Cell RNA sequencing Using Machine Learning Techniques: A Review

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ABSTRACT: In the developing nations cancer disease is one of the serious issues for humanity. One of the most widely recognized disease types is breast cancer which is known as bosom malignant growth. Despite the fact that there are numerous ways of forestalling it prior to working out, some disease types actually have no treatment. Early recognition is truly significant in its treatment. It is treatable on the off chance that it is identify on the early condition of malignant growth sickness. Precise finding is perhaps of the main cycle in the bosom disease treatment. Normal screening procedures of breast cancer are mammography, MRI, CT SCAN, USG and biopsy. Aside from these procedures single cell RNA sequencing is novel method which is utilized to distinguish malignant growth cells, new cell types and their biomarkers. In the review survey, there are many examinations about finding and expectation of bosom disease utilizing AI methods including Support Vector Machine (SVM), K-nearestneighbors (K-NN) , Naive Bayes(NB), Logistic regression(LR),Random Forest (RF), Decision tree(DT) and Artificial Neural Network(ANN),These procedures are utilized to upgrade the precision and execution. The Propose System is utilized Single cell RNA sequencing database for identifying bosom malignant growth cell utilizing ML classification for prediction and analysis.

KEYWORDS: Breast Cancer, Single cell RNA sequencing, Artificial Intelligence, Machine learning.

I. INTRODUCTION

Malignant growth (cancer) is the second greatest executioner disease in the world. In the human body system, it has been found that it can take up just about 200 distinct structures, for example, prostate, ovarian, bosom (breast cancer), lung, skin as well as hematologic disease. In particular, the fast advancement of malignant growth in the human body is set off by the natural components like radiation, smoking tobacco, a lot of liquor utilization, perilous synthetic compounds among different elements (Nobili et al., 2010).Also, disease can be set off hereditarily by acquired changes as well as immune system brokenness. Cells in the body regularly partition just when new cells are required. At times, cells in a piece of the body develop and partition wild, which makes a mass of tissue called a growth or tumor. The ordinary mass tissue (tumor) is called benign (not dangerous) and the unusual mass tissue (tumor) is called malignant (dangerous). Not with standing, a few types of disease like stomach and cervical are separately connected with bacteriological and viral contaminations. Research has uncovered that the most widely recognized type overall in both male and females are prostate and bosom malignant growth correspondingly.

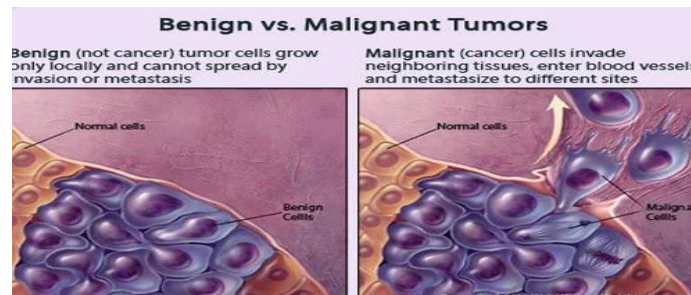


Fig 1: Normal (Benign) and abnormal (Malignant) cells

Bosom disease is a type of disease that can form in the cells of breast. Bosom disease arises in both rural and metropolitan in India. A 2018 report of Breast Cancer measurements recorded 1,62,468 new enlisted cases and 87,090 detailed passing, it is the most successive threat in ladies overall and is reparable in 70-80% of patients with beginning phase, non-metastatic sickness.[5]

More than 1.3 million ladies overall are determined to have bosom disease every year, making it the most well-known type of malignant growth.

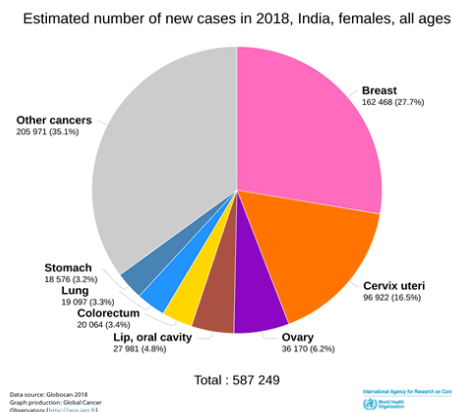


Fig 2: Cancer Statistics in India (2018)

There are various cancer screening methods are available such as Mammogram,3D Mammogram, Ultra Sound ,MRI,MBI,CT Scan, Blood Profiling through biopsy and Gene Expression (Genome Sequencing, RNA Seq.).

➤ **Statement of Problem**

The traditional screening techniques has some limitations such as

- **Mammogram:** This is a kind of X-ray that specialists generally use during an underlying bosom malignant growth screening.
- Mammograms have their cutoff points. For instance, they aren't 100 percent exact in appearing in the event that a lady has bosom malignant growth
- A **false-negative** mammogram looks typical despite the fact that bosom malignant growth is available.
- **Ultrasound:** Numerous malignant growths are not apparent on ultrasound.
- **MRI:**It isn't generally ready to recognize the contrast between carcinogenic anomalies, which might prompt superfluous bosom biopsies. This is frequently alluded to as a "false positive" test result.
- **CT Scan:** The significant restriction of CT Scan for bosom imaging is its unfortunate location rate for little bosom carcinomas and painless bosom diseases.
- Apart from these screening some other screenings are most expensive and painful.

Due to beat this large number of restrictions, a high-level procedure has been presented, for example Next Generation Sequencing technique. in which Gene expression, Sequencing technique are the arising innovation to recognize malignant growth followed by the advancement of computational tools have empowered examinations like entire

whole-exome sequencing (WES), Whole-genome sequencing (WGS) and RNA-sequencing (RNA-seq). RNA sequencing (RNA-seq.) is quite possibly of the most ordinarily involved procedure in life sciences, and has been broadly utilized in disease research, drug improvement, and disease determination and prognosis. RNA sequencing gives useful information about malignant growth gene expression and the gene fusion that drive cancer movement. There are various kinds of RNA sequencing procedures, for example, Bulk RNA-seq., Laser-captured micro-dissected RNA-seq., digital spatial RNA profiling, Spatial transcriptomics, and Single-cell RNA-seq. Single-cell RNA sequencing (sc-RNA-seq.), an innovation that dissects transcriptomes of perplexing tissues at single-cell levels, can distinguish differential gene expression and epigenetic factors brought about by changes in unicellular genomes, as well as new cell-explicit markers and cell types.

Single-cell RNA sequencing (scRNA-seq) is looking at RNA in every individual cell of an example independently and has in this manner changed how we might interpret the heterogeneity of individual cells. scRNA-seq assumes a significant part in different parts of cancer research. (scRNA-seq) conquers the restrictions of conventional RNA sequencing strategies by estimating the entire transcriptome at a solitary cell goal and recognizing different cell types in growth tissue [3]. To recognize and investigate this gene expression utilizing, different ML classification techniques are utilized. Following literature review examine different AI & ML methods for the discovery and investigation of the bosom disease cells.

II. LITERATURE REVIEW

The fundamental focal point of this study is to foster an intelligent framework utilizing AI & ML models for an early detection of the bosom disease cells from the patient's information. Through the literature review, were finished applying and utilizing a few ML classifiers to decide on early findings and forecast of bosom malignant growth utilizing ML methods are discussed below;

Sr. No	Author	Title & Year	Journals	Methodology
1.	Marco Del Giudice , Serena Peirone ,Sarah Perrone ,Francesca Priante ,Fabiola Varese	“Artificial Intelligence in Bulk and Single-Cell RNA-Sequencing Data to Foster Precision Oncology”(2021)	Int. Jr. Molecular Science	In this paper, the author outlines AI approaches applied to bulk and single-cell RNA-seq. in malignant growth genomics and accuracy oncology. They make sense of unmistakable methodologies for facing the "heterogeneity challenge". They can frame a portion of the significant commitments of applying AI to the necessities of malignant growth genomics, from distinguishing uncommon disease subtypes to customizing treatment for people.
2.	Guangshun Sun,1,2,6 Zhouxiao Li,3,6 Dawei Rong,4,6 Hao Zhang,1,5,6 Xuesong Shi,2 Weijun Yang,2 Wubin Zheng,2	“Single-cell RNA sequencing in cancer: Applications, advances, and emerging challenges”(2021)	Molecular Therapy: Oncolytics Vol. 21 June 2021	This survey sums up the examination progress of scRNA-seq in the field of cancers, zeroing in on the utilization of scRNA-seq in growth circling cells, cancer immature microorganisms, growth drug opposition, the cancer microenvironment etc., which gives another viewpoint to cancer research.
3.	Silvia Cascianelli, Ivan Molineris , Claudio Isella , Marco Masseroli & Enzo Medico	,”Machine learning for RNA sequencing based intrinsic subtyping of breast cancer”(2020)	Scientific Reports (2020) 10:14071	Author work on two dataset TCGA and GSE96058 data and applied ML algorithms such as (1) Decision Forest; (2) Decision Jungle; (3) Logistic Regression (LR); (4) Feed-Forward Neural Network (FFNN); (5) Support Vector Machines (SVMs). LR classifier has the best accuracy among others with 88% on TCGA and 85% on GSE96058.

4.	Zhezhou Yu, Zhuo Wang, Xiangchun Yu, Zhe Zhang	“RNA-Seq-Based Breast Cancer Subtypes Classification Using Machine Learning Approaches” (2020)	Computational Intelligence and Neuroscience	Author work on RNA-Seq. based gene expression data of BRCA was downloaded from the TCGA database. In this research they are used three ML classifiers such as NB, RF and SVM Radial. RF and SVM have the best accuracy and sensitivity. Table 3 shows all subtypes of breast cancer with classifiers.
5.	Ye Wang, Michael Mashock, Zhuang Tong, Xiaofeng Mu ^{1,4} , Hong Chen ⁵ .	“Changing Technologies of RNA Sequencing and Their Applications in Clinical Oncology”(2020)	Frontiers in Oncology	Author presents different RNA seq procedures, for example, mass RNAseq, laser-caught miniature analyzed RNAseq, and single-cell RNAseq to advanced spatial RNA profiling, spatial transcriptomics, and direct in situ sequencing. These various advancements have their extraordinary assets, shortcomings, and appropriate applications in the field of clinical oncology.
6.	Noreen Fatima, Li Liu, Sha Hong, And Haroon Ahmed	“Prediction of Breast Cancer, Comparative Review of Machine Learning Techniques, and Their Analysis “ (2020)	IEEE open ACCESS JOURNAL	This article presents the relative investigation of AI, profound learning and information digging procedures being utilized to expect bosom malignant growth. Calculations, for example, Random Forest, Naive Bayes, Support Vector Machine and K Nearest Neighbor were relatively utilized by creators on WDBC and WPBC datasets. They utilized a MATLAB tool to group information concerning their precision accurately.
7.	F. M. Javed Mehedi Shamrat	”An Analysis On Breast Disease Prediction Using Machine Learning Approaches”(2020)	IJSTR(International journal of scientific & technology research)	In this study, Author uses the Wisconsin Breast Cancer dataset and applied ML classifiers such as Naïve Bayes, Random Forest, Support Vector Machine, Decision Tree, KNN and Logistics Regression algorithms. The results evidently show that the DT and LR reached to the highest precision (97%) among other classifiers.
8.	Anji Reddy Vaka, Badal Soni, Sudheer Reddy K	“Breast cancer detection by leveraging Machine Learning”(2020)	ICT EXPRESS & ELSEVIER JR.	The authors present the new method DNNS with SVM, NB, RCNN, HA-BIRNN for detecting Breast Cancer. Unlike other methods, the proposed method is based on Support value on a deep neural network. Experimental results proved that the proposed DNNS is quite better than the existing methods. It is ensured that the proposed algorithm is advantageous in both performance, efficiency and qualities of images are crucial in the latest medical systems.
9.	Siham A. Mohammed, Sadeq Darrab, Salah A. Noaman, Gunter Saake	“Analysis of Breast Cancer Detection Using Different Machine Learning Techniques”(2020)	SPRINGER	Author utilized three unique classifiers: Decision Tree (J48), Naïve Bayes (NB), and Sequential Minimal Optimization (SMO). Validate and think about the classifiers on two benchmark datasets: Wisconsin Breast Cancer (WBC) and the Breast Cancer dataset. The outcomes show that J48 (Decision Tree) is the best one with 75.52% exactness, where the precision of NB and SMO are 71.67% and 69.58%, individually.
10	Anoy Chowdhury	“Breast Cancer Detection and Prediction using Machine Learning” (2020)	Research Gate	Author utilized the Wisconsin bosom disease dataset and applied 5 AI models, for example, Decision tree (kNN), SVM, Naïve Bayes, and Logistic relapse on the dataset. Choice Tree Classifier has the best exactness among the whole models ie.96.5%.

11	Kevin Menden\$ 3 , Mohamed Marouf, Sergio Oller, AnupriyaDalmi a, Karin Kloiber,	“Deep-learning-based cell composition analysis from tissue expression profiles”(2019)	SCIENCE ADVANCES	The author utilizes a Deep Neural Network for cell deconvolution that utilizes quality articulation data to derive the cell arrangement of tissues. They work prepared on single cell RNA-sequencing information to design discriminative elements that present strength.
12	<u>Xiaoning Tang, Yongmei Huang, Jinli Lei, Hui Luo & Xiao Zhu</u>	“The single-cell sequencing: new developments and medical applications.” (2019)	Springer	This review introduces the latest advances in single-cell sequencing technologies and their applications in oncology, microbiology, neurology, reproduction, immunology, digestive and urinary systems, highlighting the important role that single-cell sequencing techniques play in these areas.
13	Shailendra Dwivedi1 • Purvi Purohit1 • Radhieka Misra2 • Malavika Lingeswaran1 • Jeewan Ram Vishnoi3	“Single Cell Omics of Breast Cancer: An Update on Characterization and Diagnosis” (2019)	Springer	Creator presented novel updates of different strategies accessible to investigate omics, and afterwards, we at long last pinpointed different omics (for example, genomics, transcriptomics, epigenomics, proteomics and metabolomics) information and barely any extraordinary parts of coursing growth cells, scattered cancer cells and disease immature microorganisms, so far accessible from different investigations that can be utilized for better administration of bosom disease patients.
14	Shreshtha Malvia1, Sarangadhara Appala Raju Bagadi 1, Dibyabhaba Pradhan2, ChintamaniChintamani 3..	“Study of Gene Expression Profiles of Breast Cancers in Indian Women “ (2019)	Scientific Reports 9:10018 https://doi.org/10.1038/s41598-019-46261-1	To comprehend the sub-atomic cycles hidden bosom disease in Indian ladies, dissected quality articulation profiles of 29 growths and 9 controls utilizing microarray. In the current review, we got 2413 differentially communicated qualities. These study reports quality articulation profiles of bosom growths from the Indian subcontinent, illuminating the pathways and qualities related to bosom tumorigenesis in Indian women. They utilized unaided grouping techniques to examine the qualities.
15	M. Tahmooresi1 , A. Afshar , B. Bashari Rad , K. B. Nowshath1 and M. A. Bamiah	“Early Detection of Breast Cancer Using Machine Learning Techniques”(2018)	Journal of Telecommunication, Electronic and Computer Engineering	Author have study on several ML algorithms including SVM ,(ANN), K-NN,GMM,,LRC,NB,DT etc. on various types of database for effective breast cancer detection.
16	Quy H. Nguyen1 , Nicholas Pervolarakis2, Kerrigan Blake2, Dennis Ma1 , Ryan Tevia Davis3...	“Profiling human breast epithelial cells using single cell RNA sequencing identifies cell diversity” (2018)	NATURE COMMUNICATIONS DOI: 10.1038/s41467-018-04334-1	Author utilized single-cell mRNA sequencing (sc-RNA-seq.) to profile the transcriptomes of 25,790 essential human bosom epithelial cells secluded from decreased mammoplasties of seven people. Unprejudiced grouping examination uncovers the presence of three particular epithelial cell populaces.

The principal reason for this study is to inspect the performance of different leading supervised and unsupervised ML classifiers that have obtained highest accuracies in the field of disease prediction and acquired proficient results. The relative investigation of this study is the most reliable outcome among other ML algorithms for bosom malignant growth prediction: Random Forest, Decision Tree, Support Vector Machine and K Nearest Neighbors.

III. OBJECTIVES OF THE STUDY

1. To study various types of screening techniques.
2. To find new technology for early detection of breast cancer.
3. To identify markers of breast cancer genes using Single cell RNA sequencing dataset.
4. To apply Machine Learning classification for prediction and empowers accurate results.

IV. METHODOLOGY

The outline of literature review AI and ML approaches applied on the different datasets to track down gene expression for diagnosis and prognosis of bosom malignant growth cells. They give a near examination of AI, Deep learning and data mining methods being utilized for bosom malignant growth discovery. Different direct AI algorithms are utilized for grouping, for example, Logistic Regression, K-NN, SVM, Naïve Bayes, Decision Tree, and Random Forest. Supervised AI algorithms for recognized data by sorting out the given data and making assumptions about the future .Classification and regression are two distinct categories under these methodologies. Classification is a method to decide the mark of the information utilized for various reactions, in contrast to the regression technique. In the classification process, the initial step is to peruse the given dataset. Different classification algorithms are typically liked for AI applications. These classification algorithms were utilized to make accurate score. Every classification is applied to the different datasets that incorporate different features. Researchers are used different datasets, for example, WBCD, TCGA, GSE, GEO, ICGC, etc.

The proposed framework utilized single cell RNA sequencing data from online open source dataset such as, Gene Expression Omnibus (GEO) is a database for gene expression profiling and high through put RNA seq. experimental data,The cancer Genome Atlas(TCGA) have gene expression data.

Following figure shows the conceptual work flow of proposed system.

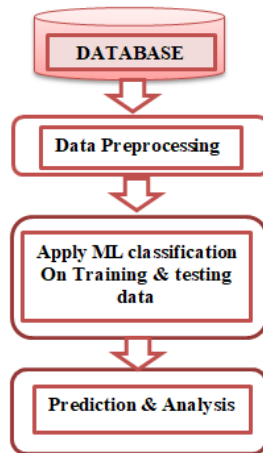


Fig 3: Proposed System Workflow

The initial step of the proposed framework is an assortment of data from the online data source talked about above .and second step is doing some preprocessing steps on the given dataset such as removing unwanted data and missing values from the database. The third step is splitting data into training and testing dataset for the ML classification process. Proposed system used SVM, DT, RF and K-NN classifiers for detecting and analyzing of breast cancer genes.

V. CONCLUSION AND FUTURE WORK

In the Literature audit, I had gone through various AI & ML, deep learning and data mining algorithms for the prediction of bosom disease. Our primary aim is to figure out the most suitable classifier to anticipate the events of bosom disease all the more real. The primary motivation behind this literature study is to feature every one of the past investigations of AI algorithm that are being utilized for bosom disease prediction. The survey of this literature is begun from the sorts of bosom malignant growth; some research papers have been evaluated to get some information about the significant kinds, side effects and reasons for bosom malignant growth. From that point onward, the survey of significant AI procedures K-NN, SVM, Decision Tree, and Random Forest has been given the methods profoundly elaborate calculations that are being utilized for the expectations of bosom malignant growth. We can increase the number of ML algorithms and analyze the performance.

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