2022 IEEE 2nd International Conference on Mobile Networks and Wireless Communications (ICMNWC)

Prediction of Early Stage Breast Cancer by Injection of Gold Nano Particles and Analyzing Images using Data Analytics

1st Sreevidya Nelli
Department of Information Technology
Sreenidhi Institute of Science and Technology
Hyderabad, India
sreevidyan@sreenidhi.edu.in

2nd Kezia Rani B.
Department of Computer Science and Engineering
University College of Engineering
Rajamahendravaram, India
kezia.cse@aknu.edu.in

2022 IEEE 2nd International Conference on Mobile Networks and Wireless Communications (ICMNWC) | 978-1-6654-9111-2/22/$31.00 ©2022 IEEE | DOI: 10.1109/ICMNWC56175.2022.10031956

Abstract—According to recent studies, breast cancer is the most common cancer among women, and its prevalence is steadily increasing. An early diagnosis and treatment of this condition can greatly increase the chances of a cure. Further, Long-term mortality rates from breast cancer dramatically lowered by early cancer identification. Finding cancer cells in their early stages is the most important step for the best prognosis. Researchers have examined a variety of breast diagnostic techniques, including mammography, ultrasound, positron emission tomography, and biopsy. These methods have some drawbacks, though, such the fact that they are expensive, time-consuming, and unsuitable for young women. Therefore, it is vital to create a quick and sensitive early-stage breast cancer diagnosis tool. Recently, the rapid advancement of nanotechnology has increased research on nanoparticles, especially those that can be applied to the medical field. Gold nanoparticles (AuNPs) are continuously being studied and used as tools for further research resulting in ever-expanding knowledge that constantly challenges the frontiers of nanotechnology. An increasing interest is being manifested in the use of AuNPs to treat cancer, from diagnosis and monitoring through to treatment. Cancer is a multifactorial disease that requires multifaceted treatments, so these efforts aim to revolutionize current methods of treating it. In this review, the current applications of AuNPs in early breast cancer diagnosis and the importance of biosensors in predicting early cancer occurrence are discussed.

Keywords—Gold nanoparticles, Breast cancer, Cancer imaging, Cancer treatment, Data Analytic.

I. Introduction

The "Global Breast Cancer Statistics" report shows breast cancer is the most common form of cancer among women, accounting for 23% of all cancer [1]. Only 60% of women, who are treated for breast cancer, survive for at least five years post-treatment in India as compared to 89% in the US. The existing and popular methods like Mammograms, MRI, Compound Imaging, Ultrasonography etc. can detect the disease at stage 3 or stage 4(Metastasis). Therefore, it is imperative to detect breast cancer in the early stages of the disease. The early detection of cancer can be achieved with a simple blood test [2]. The detection of the advanced stages of cancer is quite complicated and expensive. CancerSeek is a liquid biopsy test that can detect cancer with the help of alterations in 16 genes and the circulating tumor DNA present in the bloodstream related to cancer. CancerSeek resulted in more than 99% in terms of specificity. But a blood test alone cannot identify and confirm cancer without performing screening tests. Galleri is a new blood test 1which can detect more than 50 types of cancer through a single blood draw and can detect early stages of cancer before a person has symptoms [3]. Any blood test needs to combine with standard screening tests like Mammography, Clinical Breast Exam, and Breast MRI for better confirmation [4].

In addition to blood tests, imaging methods like SPECT (Single Photon Emission Computed Tomography) and PET (Positron Emission Tomography) scans are needed for the diagnosis of cancer. As nanoparticles have been widely used in the treatment of breast cancer because of their property to detect tumor cells without affecting the healthy cells and nanoparticles can also be used in the methodology of detecting cancer [5]. As a result, nanoparticles have an enormous range of applications in medical and pharmaceutical areas, as well as controlled delivery of drugs. Out of all inorganic nanoparticles, gold has been in wide use, in Drug delivery, Cancer Treatment etc., and is effectively used in the treatment of cancer by targeting the tumor cells. It can be used in the detection of cancer at the early stages without destroying healthy cells. Till now the biomarkers like Circulating Tumor DNA's and other biomarkers were used to detect cancer cells. As the tumors shed layers cancer cells can be detected at an early stage using gold nanoparticles based on CTC's. Detecting circulating tumor cells (CTCs) in the bloodstream early can have an impact on cancer prognosis. CTCs are very rare and CellSearch is the only approved USFDA (United States Food and Drug Administration) method to detect these in the bloodstream. So, this method can be used to detect CTC's and CTC's confirm the cancer cells and their location [6]. After confirming the cancer cells, various methods can be applied to compare the images obtained before and after the detection of CTC's by using the techniques of Artificial Intelligence, Deep Learning, Data Analysis combined with classification algorithms.

Depending on the size of the tumor identified, and based on the results of all the algorithms and techniques, the best algorithm will be used to detect cancer. And, based on the result, we can also determine the stage of cancer (Stage 1/2/3). If the tumor is detected at any of these stages, it is indicative of detecting cancer at an early stage. So, when the cancer is detected at an early stage, the chances of curing are high, and treatment can also be started at an early stage. so, the people suffering from this disease can be identified in the preliminary stages using this technique and we can save millions of lives worldwide thereby reducing the mortality rate. As long as this technique achieves the best results and the highest percentage of efficiency, it could become a new technique for detecting breast cancer at an early stage.

II. Related Works

Traditional methods like Mammograms, Ultrasound and CAD etc. can detect breast cancer only at stage 3 or stage 4 (metastasis). Therefore, early detection and treatment are crucial to increase the chances of survival. By using machine learning, artificial intelligence, data analytics, and big data, data mining, machine learning, and artificial intelligence have been an invaluable tools for this research. We presented a model that predicts breast cancer based on machine learning and biosensor models.

For early breast cancer detection, Siham et al. [7] used Wisconsin Breast Cancer datasets and breast cancer datasets from the National Cancer Institute (NCI). First of all, the three classification algorithms J48, NB, and SMO were tested without preprocessing the datasets. J48 ranked highest in the breast cancer dataset at 75.52 %, followed by SMO at 96.5 %. With the application of pre-processing techniques like discretization, resampling, and removal of missing values, the accuracy of the breast cancer dataset increased to 98.20% with J48, and 99.56% with SMO.

Gold nanoparticles (AuNPs) have been shown to assist in cancer diagnosis, monitoring and treatment, according to a recent study Jingwen Peng et.al [8]. As a drug delivery agent or in gene therapy, AuNPs could be used to target cancer cells. According to the author, single photon emission computed tomography (SPECT) and positron emission tomography (PET) both have higher sensitivity and specificity when separating tumours from normal tissues, yet their spatial resolution is poor. As a result of their highly stable synthesis, high X-ray absorption capabilities, and mature synthesis, AuNPs have become increasingly popular. Despite the limitations of the tumour imaging and radio-sensitization studies of AuNPs, they provide new strategies for early diagnosis and precise treatment. In addition to their small size, high atomic number, and good biocompatibility, tiny AuNPs make excellent contrast agents. Active targeting uses the osmotic tension effect (EPR) to converge the AuNPs in tumour tissue to enhance imaging. When AuNPs are coupled with monoclonal antibodies, gene-targeting GNPs can be active against cancer cells by targeting EGFR (Epidermal Growth Factor Receptor). Iodine has a lower mass decay when the energy exceeds 80 keV, meaning gold nano will be more advantageous for development and manufacturing.

Mukerjee et al. [9] mentioned that gold nanoparticles can be used in photothermal therapy. Photothermal therapy can therefore be carried out using these materials due to their unique surface plasmon resonances. They convert light into heat and kill cancerous cells. In a study by Rand et al. [10], gold nanoparticles were mixed with liver cancer cells and X-ray imaging was used to determine if gold nanoparticle-mixed liver cancer cells were more potent than simple liver cancer cells. New technologies are allowing the detection of tumors of a few millimeters in diameter in vivo, which was extremely significant for early diagnosis.

A bioconjugate based on Hyd-AuNP-Apt (Hydrazine-Au Nanoparticle-Aptamer) was developed by Ye Zhu et al. [11] for the first detection of the HER2 protein and SK-BR-3 breast cancer cells. Usi, g this sensor, researchers were able to detect SK-BR-3breast cancer cells with an accuracy of 26 cells/ml while discriminating between HER2-positive and HER2-negative cells.

Lee et al. [12] say that gold nanoparticles have these properties shown in fig.1.

A tumor carries nanoparticles with Enhanced Permeability and Retention (EPR) that can be either activated with light, delivered drugs/DNA, or both. These strategies can be used to treat cancer. Many issues need to be resolved in AuNP research due to their infancy, including reducing toxicity while improving stability. In this review, we summarize recent developments in nanotechnology-based cancer diagnosis (Figure. 2)[13].

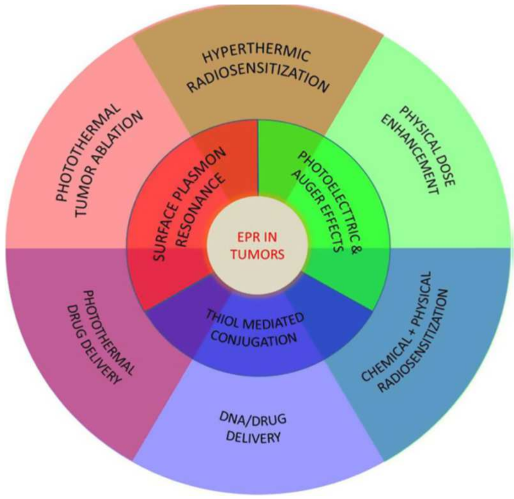

Fig. 1. Properties of gold nanoparticles and their potential use in cancer treatment.

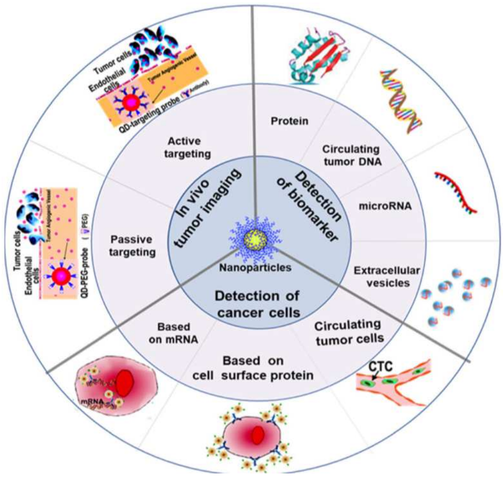

Fig. 2. Taxonomy of nanotechnology applications in cancer diagnosis [13]

III. Problem Statement

Researchers are using nanoparticles to identify cancer biomarkers such as cancer-associated proteins, circulating tumour cells, and exosomes [13].

- As a cancer biomarker, a molecule found in blood, other body tissues, or body fluids such as saliva or urine can identify cancer in the body. Cancer can be detected by circulating tumour DNA, miRNA, or secreted proteins (cell surface proteins) or nucleic acids (secreted proteins or cell surface proteins). Detecting cancer biomarker levels early and monitoring the efficacy of therapies are two of the benefits of measuring cancer biomarker levels [13].
- Detection of circulating tumour cells (CTCs) in the bloodstream can significantly improve cancer diagnosis and outcome. Nanotechnology has been applied to the detection of CTCs recently for the sensitive detection of these cells; a wide range of clinical applications can be realized through these technologies, including early disease detection,

treatment evaluation, and disease development monitoring. [13]

Among the nanoparticle probes used to diagnose cancer, three types can be distinguished: quantum dots (QDs), gold nanoparticles (AuNPs), and polymer dots (PDs). Research is being conducted on both quantum dots and polymer dots for breast cancer detection. AuNPs have a number of properties such as their small size, their ability to penetrate and deposit at tumor sites, and their high biocompatibility, making the detection of breast cancer via AuNPs a future possibility. By detecting CTCs, we can cure women of cancer in the early stages, leading to a lower mortality rate, because cancer cells can be detected at an early stage.

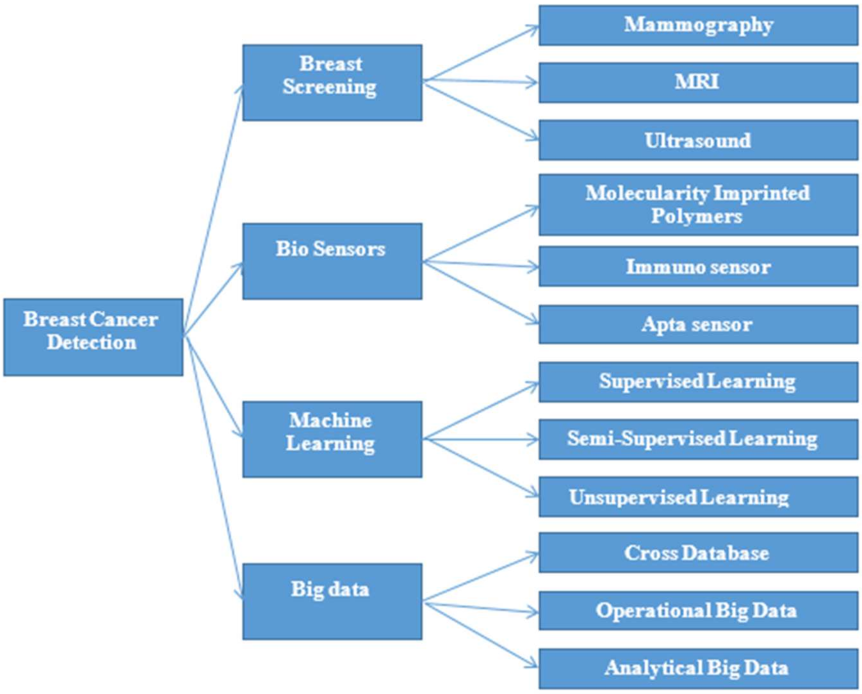

Fig. 3. Taxonomy of Breast Cancer Detection in Different Stages

As modern medicine has progressed, certain technological advancements have been applied to breast cancer detection. Figure 3 illustrates the major ones.

A. Breast screening techniques

Early identification of diseases is possible through breast screening before symptoms develop. Genetic testing to identify inherited diseases and physical examinations, such as imaging or physical exams, are examples of screening tests that can be performed as part of a screening test. Mammograms, MRIs, whole-slide imaging (WSI), and ultrasounds are some of the screening modalities.

B. Biosensors

Biosensors are devices that measure the biological characteristics of body fluids and tissues. An example of a biosensor are optical biosensors, piezoelectric biosensor, or electrochemical biosensor.

C. Machine learning

Machine learning offers unique advantages in detecting critical features from the overall complex datasets when it comes to breast cancer pattern classification and decision prediction. The classification of data can be accomplished with KNN, SVM, and DT based methods. In addition, these methods are highly helpful in identifying and determining clinical conditions.

D. Big Data analysis

Methods based on Big Data allow experts to rely on unstructured information, including textual reports from patients and images, to influence clinical decision making and ultimately patient care. Big Data can be analyzed in several ways, including cross-database analysis, analytic big data analysis, and operational big data analysis.

Applications of AuNPs in cancer management

Recent years have seen a significant increase in interest in gold nanoparticles because of their unique physical and chemical properties, which makes them suitable for drug delivery due to their large surface area to volume ratio. Here are two major uses of gold nanoparticles.The analysis of Au NP shown in Fig. 4.

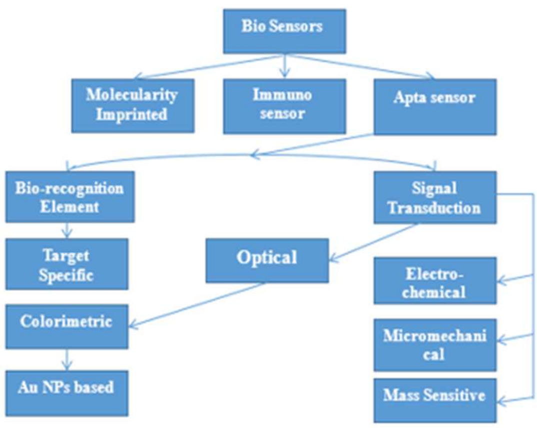

Fig. 4. Au NP Analysis

Gold NP as Biosensor: Since AuNPs interact with visible light strongly, they are ideal candidates for labelling applications. Gold exhibits the ability to reflect and absorb visible light when it is exposed to light via surface plasmon resonance (SPR) caused by free electrons in its atoms. It is imperative to monitor cancer early and use AuNPs as imaging probes for early detection. AuNPs, with their great optical scattering properties, is a good choice due to their biocompatibility and relative strength. Molecular markers such as AuNPs are capable of identifying tumor cells by combining antibodies with antigens present in cancer cells. This enables the precise location of the tumors in the body. Surface-enhanced Raman spectroscopy (SERS) has been studied as a technique to detect biomarkers expressed in breast cancer cells by antibody-conjugated hollow gold nanospheres. Detection of breast cancer in the early stages is supported by early detection models.

Gold NP as drug Delivery: AuNPs have several uses, including their use as a vehicle for delivering molecules to cells. In preclinical studies, the carrier molecule was found to be potentially therapeutic due to its easy synthesis and functionalization, relative biocompatibility, and low toxicity. The design of an efficient drug delivery system must take into account a number of factors. AuNPs are affected by their size, charge, and surface chemistry, as well as their ability to penetrate cells and enter the cell's interior. Gold nanoparticles are used in clinical drug delivery. To produce high therapeutic efficacy, AuNP needs to be controlled to ensure the strongest drug attachment and release timing. AuNP is attractive for drug delivery due to its ability to modify its surface.

Table I represents performance analysis of AU in sensor and drug delivery.

TABLE I. PERFORMANCE ANALYSIS OF AU IN SENSOR AND DRUG DELIVERY

Reference	Type	Drug and NP	Outcome
López-Marzo (2018) [14]	Bio Sensor	SPCE/AB/Au	Detection Limit: 0.06 ng/mL Electrochemical indicators
Bao, J (2018) [15]		GCE/AuNPs/CP	Detection Limit: 0.5 ng/mL Electron migration enhancers
Zhu, D.M et.al (2018) [16]	Drug Delivery	Paclitaxel (PTX) / Au	Possible targeting toward cancer cells and NIR-stimulated release of PTX.
Ali, M.M et.al (2020) [17]		Etoposide (ETP) / Au	Improved cytotoxicity compared to free etoposide

IV. APPLICATIONS OF MACHINE LEARNING IN CANCER MANAGEMENT

A subfield of artificial intelligence (AI) is machine learning, which employs soft coding instead of hard coding. An example of ML would be a machine that continues to gain knowledge despite the absence of explicit programming instructions. There's a long history of ML models' helping cancer researchers with both research as well as practical implementation. CADe systems are used to detect clinically significant objects, while CADx systems determine whether an object is malignant automatically or manually. The primary benefit of using these algorithms and techniques is their superior accuracy in classifying breast cancer in its early stages. This is one of the reasons why many studies have used data mining algorithms and techniques to do so. These efforts led to many researchers focusing on solving complex and challenging tasks using self-learning, mining and computing models that use machine learning techniques.

Unsupervised learning: This techniques effectively identify the unknown patterns in acquired data without pre-existing labels. A few examples are Deep Neural Network (DNN), autoencoder, capsule network architecture, Convolutional Neural Networks (CNN), and graph neural networks, etc.

Supervised learning: This techniques identify the unknown patterns in acquired data by pre-existing the labels. A few examples are decision trees, Support Vector Machines (SVM), Naive Bayes, etc.

Semi-supervised learning: This techniques classify the acquired data with and without using the labels, generally it falls between the category of unsupervised and supervised learning techniques. A few examples are heuristic models, generative methods, etc.

Table II represents analysis of machine learning algorithm in breast cancer detection.

TABLE II. ANALYSIS OF MACHINE LEARNING ALGORITHM IN BREAST CANCER DETECTION

Reference	Model	Task	Performance
Ribli (2018) [18]	Faster-RCNN	Classification and Detection	AUROC : 0.95
Singh (2020) [19]	cGAN	Classification and Segmentation	AUROC : 0.80 Dice: 0.94
Liang et al. (2020) [20]	CNN ensemble	Classification	AUROC : 0.87
Zhou et al. (2021) [21]	CVNET	Classification	AUROC : 0.787

V. CONCLUSION

A significant amount of research has been conducted on gold nanoparticles over the past decade that shows potential for the use of these particles in imaging and treatment of cancer. Gold nanoparticles have undergone extensive studies on their chemical synthesis and bio-behavior, allowing many practical clinical applications to be developed. In ML applications, constructing efficient and accurate classifiers that can be applied in practice is a major challenge. Most concerns in cancer cell classification can be found in the following areas: large numbers of cancer cell expressions, investigation of relevant features, noise in datasets, and classification accuracy and reliability. Researchers in computational biology are likely to reap some promising results in the future by using recent deep-learning techniques along with self-learning algorithms to check for breast cancer recurrence.

REFERENCES

[1] M. Shamsi, and J.P. Islamian, “Breast cancer: Early diagnosis and effective treatment by drug delivery tracing”, *Nuclear Medicine Review*, vol. 20, no. 1, pp. 45-48, 2017.

[2] S. Bhana, Y. Wang, and X. Huang, “Nanotechnology for enrichment and detection of circulating tumor cells”, *Nanomedicine*, vol. 10, no. 12, pp. 1973-1990, 2015.

[3] Z. Zhang, and M.R. King, “Nanomaterials for the capture and therapeutic targeting of circulating tumor cells”, *Cellular and molecular bioengineering*, vol. 10, no. 4, pp. 275-294, 2017.

[4] H. Li, H. Li, and A. Wan, “Luminescent gold nanoclusters for in vivo tumor imaging”, *Analyst*, vol. 145, no. 2, pp. 348-363, 2020.

[5] S. Siemer, D. Wünsch, A. Khamis, Q. Lu, A. Scherberich, M. Filippi, M.P. Krafft, J. Hagemann, C. Weiss, G.B. Ding, and R.H. Stauber,

"Nano Meets Micro-Translational Nanotechnology in Medicine: Nano-Based Applications for Early Tumor Detection and Therapy", *Nanomaterials*, vol. 10, no. 2, pp. 383, 2020.

[6] Q. Huang, Y. Wang, X. Chen, Y. Wang, Z. Li, S. Du, L. Wang, and S. Chen, "Nanotechnology-based strategies for early cancer diagnosis using circulating tumor cells as a liquid biopsy", *Nanotheranostics*, vol. 2, no. 1, pp. 21, 2018.

[7] S.A. Mohammed, S. Darrab, S.A. Noaman, and G. Saake, "Analysis of breast cancer detection using different machine learning techniques", *In International Conference on Data Mining and Big Data*, pp. 108-117, 2020

[8] S.A. Mohammed, S. Darrab, S.A. Noaman, and G. Saake, "Analysis of breast cancer detection using different machine learning techniques", *In International Conference on Data Mining and Big Data*, pp. 108-117, 2020

[9] A. Mukerjee, A. Ranjan, and J. Vishwanatha, "Combinatorial nanoparticles for cancer diagnosis and therapy", *Current medicinal chemistry,* vol. 19, no. 22, pp. 3714-3721, 2012.

[10] K. Wang, C. Jin, A. Oppong-Gyebi, and J. Hu, "Application of nanotechnology in cancer diagnosis and therapy-a mini-review", *International Journal of Medical Sciences*, vol. 17, no. 18, pp. 2964, 2020.

[11] Y. Zhu, P. Chandra, and Y.B. Shim, "Ultrasensitive and selective electrochemical diagnosis of breast cancer based on a hydrazine–Au nanoparticle–aptamer bioconjugate", *Analytical chemistry*, vol. 85, no. 2, pp. 1058-1064, 2013.

[12] J. Lee, D.K. Chatterjee, M.H. Lee, and S. Krishnan, "Gold nanoparticles in breast cancer treatment: promise and potential pitfalls", *Cancer letters*, vol. 347, no. 1, pp. 46-53, 2014.

[13] Y. Zhang, M. Li, X. Gao, Y. Chen, and T. Liu, "Nanotechnology in cancer diagnosis: progress, challenges and opportunities", *Journal of hematology & oncology*, vol. 12, no. 1, pp. 1-13, 2019.

[14] A.M. López-Marzo, R. Hoyos-De-La-Torre, and E. Baldrich, "NaNO3/NaCl oxidant and Polyethylene glycol (PEG) capped gold nanoparticles (AuNPs) as a novel green route for AuNPs detection in electrochemical biosensors", *Analytical chemistry*, vol. 90, no. 6, pp. 4010-4018, 2018.

[15] J. Bao, X. Geng, C. Hou, Y. Zhao, D. Huo, Y. Wang, Z. Wang, Y. Zeng, M. Yang, and H. Fa, "A simple and universal electrochemical assay for sensitive detection of DNA methylation, methyltransferase activity and screening of inhibitors", *Journal of Electroanalytical Chemistry*, vol. 814, pp. 144-152, 2018.

[16] D.M. Zhu, W. Xie, Y.S. Xiao, M. Suo, M.H. Zan, Q.Q. Liao, X.J. Hu, L.B. Chen, B. Chen, W.T. Wu, and L.W. Ji, "Erythrocyte membrane-coated gold nanocages for targeted photothermal and chemical cancer therapy", *Nanotechnology*, vol. 29, no. 8, pp. 084002, 2018.

[17] M.M. Ali, N.A. Rajab, and A.A. Abdulrasool, "Etoposide-loaded gold nanoparticles: preparation, characterization, optimization and cytotoxicity assay", *Systematic Reviews in Pharmacy*, vol. 11, no. 2, pp. 372-381, 2020.

[18] A. Horváth, D. Ribli, P. Pollner, Z. Unger, and I. Csabai, "Detecting and classifying lesions in mammograms with deep learning," *Scientific reports*, vol. 8, no. 1, pp. 1–7, 2018.

[19] H. A. Rashwan, V. K. Singh, F. Akram, N. Pandey, S. Romani, M. M. K. Sarker, A. Saleh, M. Arquez, D. Puig, and M. Arenas, "Breast tumor segmentation and shape classification in mammograms using generative adversarial and convolutional neural network," *Expert Systems with Applications*, vol. 139, pp. 112855, 2020

[20] G. Liang, X. Wang, X. Xing, H. Blanton, T. Salem, N. Jacobs, and Y. Zhang, "Joint 2d-3d breast cancer classification," *in Proc. of 2019 IEEE International Conference on Bioinformatics and Biomedicine (BIBM). IEEE*, 2019.

[21] H. Chen, Y. Zhou, Y. Li, X. Xu, Q. Liu, S. Wang, P.-T. Yap, and D. Shen, "Multi-task learning for segmentation and classification of tumors in 3d automated breast ultrasound images," *Medical Image Analysis*, vol. 70, pp. 101918, 2021