



AI-Driven Breast Cancer Diagnosis and Holistic Care: A Sustainable Approach to Detection and Recovery

¹Nirbhay Kumar Mishra, ²Praveen Kumar

¹Research Scholar, ²Professor

¹Department of computer science and Engineering,

¹Asian International University, Sikkim, Imphal, Manipur, India

Abstract: Breast cancer is still a major concern worldwide because it affects making a diagnosis, receiving treatment and recovering long term. Ultrasonic exams now supported with machine learning can spot and keep track of changes in the heart more effectively. Still, problems related to the psychological impact of the disease and how its treatments affect patients' daily lives are very important for the outcomes. The paper looks at these issues by emphasizing that there is a need for better ways to diagnose, a personalized method of treatment and conducting more studies about rare breast cancers. It is important for future investigations to focus on better testing techniques and caring for the whole person to aid better recovery and a healthy life.

IndexTerm: Breast cancer, diagnostic methods, machine learning, psychosocial factors, quality of life, personalized care.

I. INTRODUCTION

Breast cancer is recognized as one of the main health problems affecting people throughout the world, affecting a huge number of women and meaning high pressure on health care [1]. Breast cancer is by far the most common cancer diagnosed and the second biggest reason women die from cancer globally [2]. Spite major improvements in treatment and studies, exploring where breast cancer comes from, how it is found early, how to treat it and the effects it has on people remain vital [3]. Levels of breast cancer change in different populations and places because of genetic background, what surrounds them and their way of life. Breast cancer is reported more often in developed nations, but developing countries are also seeing it rise because of changes in lifestyles, food habits and health services [4]. Many studies prove that mutations in the BRCA1 and BRCA2 genes make it more likely someone will develop breast cancer. What a person eats, how much they drink and their hormone balance also contribute to the development of cancer [5]. It is socioeconomic factors, especially receiving healthcare and access to screening, that have a big influence on how breast cancer develops and ends up for patients [6]. The condition occurs in various forms and genetic factors do not tell the whole story about the risks. If menstruation begins before the usual age, menopause is delayed or if hormone replacement therapy is involved, chances of breast cancer rise. Disease chances also increase if a person is physically inactive, overweight or uses alcohol frequently which reminds us of the importance of disease prevention [7]. On the other hand, finding out more about how genetic elements and the environment interact is still important [8]. Throughout the years, different ways to find and diagnose breast cancer have improved a great deal. Mammography, ultrasound and biopsy are still important traditional methods. Digital mammography and 3D imaging which are newer methods, have increased the accuracy of finding tumors in women with dense breasts [9]. The use of artificial intelligence (AI) and machine learning (ML) has helped improve diagnostics, as it can detect features on medical images that might go unnoticed by humans [10]. Because of these developments, doctors are better able to spot diseases, but problems such as concealed tissues and getting wrong results (false-positives or false-negatives) still exist [11]. Technology is being created using AI to tackle these matters and help with making decisions by medical staff [12]. The method of treating breast cancer is chosen according to what type, stage and molecules the tumor contains. Some of the usual methods are surgery, chemotherapy, radiation therapy and hormone therapy. New ways to treat cancer, for example targeted therapies and immunotherapy, give patients with resistant cancers new hope. Special efforts like targeting HER2 in cancer and boosting the immune system are thought to be the most effective in treating aggressive kinds of breast cancer [13]. For early-stage breast cancer, surgery is the main treatment which may be mastectomy or lumpectomy and afterwards, patients often get radiation to get rid of remaining cancer cells [14]. On the other hand, many treatments can change both a woman's body and her emotional state which underlines why treatment plans should pay attention to body image, fertility concerns and how she feels over time [15]. Breast cancer can be treated effectively with chemotherapy, though it typically brings on tiredness, nausea and hair loss. New ways of treatment try to lower these side effects without affecting how well they work [16]. Some hormone therapies, especially tamoxifen and aromatase inhibitors, are used effectively for hormone-positive cancers, yet they may lead to emotional and bone problems which must be watched carefully [17]. When immunotherapy is used together with chemotherapy, it has shown signs of success with people whose cancer is advanced or resistant to other treatments [18]. Both psychological and social aspects of breast cancer are very important in care. Many patients and their families have to deal with anxiety, depression and concerns related to their self-image. Long-lasting exhaustion, persistent pain and constant anxiety about cancer returning are some of the issues survivors often

deal with which means medical care should always address their mental health [19]. Quality-of-life (QoL) assessments, with questionnaires like EORTC QLQ-C30 and FACT-B, play a key role in measuring physical, emotional and social well-being [20]. Because of these assessments, the care plans can consider both physical and non-physical effects of the disease [21]. Because breast cancer is still a major problem, it is important to keep looking for new treatments and therapies. Developments in genetics, cell profiling, artificial intelligence (AI) and targeted treatment can greatly help improve the detection and management of cancers at an early stage. Access to healthcare should be more equal, especially in underdeveloped regions, for the worldwide fight against cancer [23]. Joining forces to focus on the patient's needs, combining medical care, technology and support will be vital to improving millions of women's health worldwide [24]

II. RELATED WORK

They collect information on the medical side of breast cancer to aide healthcare professionals with diagnosing, assessing risk and selecting treatments. They keep finding evidence for the link between changes in patient symptoms and steps taken by doctors, aiming to improve how well patients are looked after [1]. They talk about adjustments in breast cancer treatment, especially how these shifts are moving toward strategies tailored for each patient and based on solid evidence. One important finding from the review by Mokhatri-Hesari and Montazeri (2020) was that ensuring innovation and the introduction of fresh therapies are key to improving both survival rates and quality of life in breast cancer patients [2]. Nurses explain how breast cancer and its treatment influence the physical, mental and social living standards of patients. The authors found a need for work on the lasting effects of cancer on different populations and they pointed out the benefits of handling treatment side effects and providing social-emotional care. This review is meant to guide studies ahead and encourage care that prioritizes patients [3]. Between 1974 and 2007, Montazeri (2008) studied breast cancer-related quality of life by looking at its physical, emotional and social components. It covers ways to measure HRQoL with tools such as the EORTC QLQ-C30 and FACT-B and it reviews the effect of treatments like surgery, chemotherapy and hormonal therapy. It also points out that factors like age, what stage disease is at and the amount of support people get from their social network can affect HRQoL. It also points out that research is lacking in culture-related areas and long-term HRQoL effects and it mentions some new paths for future study [4]. They stress that electromagnetic methods help to improve the identification of breast cancer. They further say that more advances are needed to solve technical problems and make these methods safe and effective enough for clinics [5]. In his work, Sheppard (2007) stresses that follow-up care for breast cancer helps detect a recurrence, deals with the results of treatment such as physical side effects and addresses emotional concerns. It points out that the methods used to follow up vary a lot and that the effectiveness is also not the same. It encourages healthcare workers to deal with both the physical and emotional problems experienced by patients, so anxiety about another cancer occurs is among those. Problems related to the consistency of practices and not having enough resources are spotted. The authors suggest all follow-up procedures should be standard, healthcare professionals should collaborate and patients should be better informed to boost the success of care [6]. Fatima et al. study how well machine learning algorithms perform in predicting breast cancer. They state that research should keep going so that difficulties like uneven data and making sense of models can be resolved, helping them work effectively in hospitals [7]. They (Lim et al. 2011) look into how many women with breast cancer are affected by anxiety, pointing out that it greatly influences their quality of life. They look at what makes the problem worse such as worrying about the disease getting worse, not knowing what lies ahead and dealing with adverse treatment effects. It explores the effects of anxiety on complying with therapy and recovering and at the same time reviews the options of counseling, support groups and breathing exercises to deal with these problems. The authors call for cultural awareness in approaches and more studies to find out how well the treatments work in the long run to suit patients better [8]. Mousavi and his colleagues study how breast cancer is becoming more common in Iran and discuss the resulting difficulties. They suggest we pay more attention to preventive steps, early diagnosis and better treatments to handle the rising number of cancer cases [9]. Liberman et al. study how correctly scintimammography identifies breast cancer, what its benefits are and what medical applications it has. This indicates that we need to look into future research to determine exactly what its role is in diagnosing breast cancer [10]. Marla and Stallard (2009) do a study on how practical and safe day surgeries for breast cancer such as lumpectomies and mastectomies, are. Outcomes like how fast patients heal, what types of complications arise after surgery and their satisfaction are looked at, especially stressing the mental advantages and ease of this procedure. Economy and the improvement of healthcare resources distribution are addressed and the review also discusses the challenge of making sure patients choose wisely and receive proper care after their operation. The paper also explores how to optimize practices for day surgery and points out research areas for the future [11]. Hong and Xu (2022) give a broad overview of breast cancer, discussing the frequency of the condition around the world, different risk factors and genetic as well as environmental causes. They compare new tools for disease identification, for example molecular profiling and imaging and the latest therapies, for instance immunotherapy. Authors describe difficulties like metastasis, treatment resistance and unequal access to healthcare and point out how precision oncology may benefit patients. They ask for more studies and fairness in healthcare for these people to be tackled [12]. Jansen et al. (2014) studied the possible link between breast size and breast cancer, plus looked at how breast size might be important for imaging and decisions about issues such as mastectomy and reconstructive surgery. They point out how research findings are sometimes unclear and why more studies are needed to sort out these issues and improve both diagnosis and treatment methods [13]. The authors (Puliti et al., 2012) discuss the topic of overdiagnosis in mammography in Europe, showing that slow-growing tumors are sometimes found and may not need to be treated. They look into the problems caused by overdiagnosis, for example, pointless treatments, distress to patients and higher health expenses. The papers call for better screening processes, for example, by using modern diagnostic tools and categorizing patients according to their cancer risks, so they can pay more attention to cancers that may cause health problems [14]. Islam and colleagues (2014) studied what makes it difficult for breast cancer survivors to resume employment, suggesting that tiredness, pain and difficulties with mental health may be obstacles. Harassment policies mention how accommodations in the workplace can help such as flexible scheduling. Researchers also note that financial difficulties can affect recovering workers which is why family, friends and healthcare providers' support helps people recover and succeed in their work [15]. In their study, Gardezi et al. (2019) study changes in breast cancer detection using mammographies, especially through digital mammography and 3D imaging to enhance the diagnosis. It explains how using artificial intelligence and machine learning helps better visual analysis and decrease false negatives. Such difficulties are described, for example, overlapping tissues and false positives which point to the importance of more research to help mammographic technologies and their clinical usage [16]. In Paraskevi's (2012) work, the effect of breast cancer treatment on

QoL is analyzed, particularly for physical, emotional and social areas. It introduces usual QoL assessment methods, for example, the EORTC QLQ-C30 and FACT-B and examines ongoing impacts of treatments such as surgery, chemotherapy and radiotherapy. Incorporating Quality of Life (QoL) assessments is promoted by the author as valuable for managing patients [17]. In their study, Haddou Rahou and his team (2016) look at how Arab women with breast cancer experience QoL, noting problems with fatigue, anxiety and being stigmatized by society. They look at how the constraints of culture and lack of healthcare prevent people from getting medical care and use the EORTC QLQ-C30 and FACT-B tools. This population requires culturally matching interventions and studies to enhance their psychosocial care and quality of life, say the authors [18]. Mourouti and colleagues (2015) study whether different types of food and nutrients can have an effect on the risk of breast cancer. They advise that getting a proper nutritional balance might decrease the risk of disease and also point out problems in current research, so more investigations are needed to solve these [19]. The paper by Magai et al. (2007) looks into the psychosocial influences on whether women follow the recommendations for breast cancer screening and treatment such as emotional, mental and social ones. Fear, traditional ideas about health and lack of help are mentioned as barriers, so they advocate for addressing them to encourage more people to join early detection and treatment programs [20]. In their study (2019), Hosni et al. examine how ensemble classifiers can be used in breast cancer diagnostics to increase the accuracy of systems. These techniques are demonstrated such as bagging and boosting and their support in handling classes with different sizes. The authors say that more work needs to be done on these methods in order for them to be effective in medical practice [21]. Zerouaoui and Idri's work (2021) covers how modern breast cancer imaging makes use of machine learning and image processing techniques. They deal with matters such as how well data is gathered and how to improve the models, while pointing out how these technologies may help in getting accurate diagnoses and useful advice for doctors [22]. Marshall et al. (1994) cover ectopic breast cancer, a rare occurrence, by reviewing how it appears in patients, is diagnosed and can be managed. This study discusses how ectopic breast tissue is hard to find and gives helpful advice for handling such cases to increase awareness and better results [23]. Emilee and her team (2010) discuss the effects of breast cancer on women's sexual well-being, covering how treatment can change sexual function, how women see themselves and their relationships with partners. They support more counseling and complete care to help people deal with these problems and better their sexual lives [24]. A research team (Yassin et al. in 2018) analyzes how machine learning is applied in the imaging-based diagnosis of breast cancer, making use of mammography, ultrasound and MRI. They underline how it may enhance diagnosing diseases early and discuss the challenges such as finding big amounts of reliable data to train the models. The authors believe it is important to continue research to improve these methods for clinical practice [25].

III. METHODOLOGY

A. Overview

This review relies on doing a comprehensive review, synthesizing systematic reviews, carrying out a comparative analysis and coding themes. Information from 25 published peer-reviewed studies is studied from 2003 to 2025 focuses on diagnostics, various approaches to treating breast cancer, machine learning use and the psychological effects for patients.

B. Methodology Steps

1. Literature Collection

Medical articles were retrieved from PubMed, IEEE Xplore, ScienceDirect, SpringerLink and JAMA.

Grasp ideas related to breast cancer by looking for: diagnosis, machine learning, treatment, quality of life or survivorship.

Inclusion Criteria:

- Peer-reviewed publications
- English language
- Books in the series were published throughout the period 2003–2025
- Put most of your efforts into breast cancer (clinical, technical or psychosocial).

2. Categorization Framework

Studies were categorized by:

Research Type: Systematic Review, Meta-Analysis, Case Study, Technical Survey

Focus Area: Diagnosis, Treatment, Imaging, ML Techniques, Quality of Life, Epidemiology

Methodological Tools: Mammography, MRI, ML Algorithms, QoL Scales (e.g., EORTC QLQ-C30)

3. Parameter Extraction

The following was taken from each paper:

Study Objective

Methodology

The Methods and Tools That Are Used

Dataset/Population

Important Findings and What Was Achieved

Store-bought food or drink usually contains less nutrients.

4. Visualization and Analysis

All the data is now organized so that it can be reviewed.

Bar Charts showed how often each methodology was used.

Pie Charts help show how much resources patients spend on different services

Both these chart types linked the approach used to integrate focus areas.

My work involved Python (matplotlib, seaborn), along with Excel. The below Fig [1] shows the architecture diagram visually explaining Review methodology.

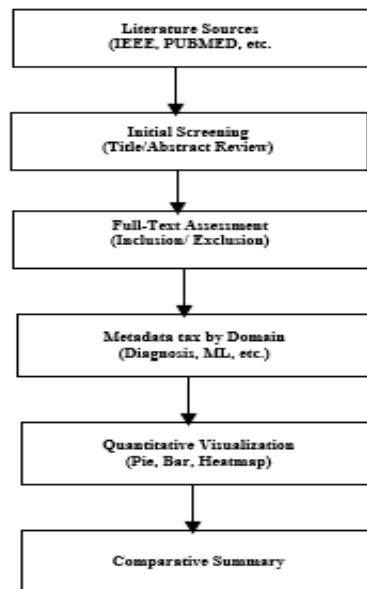


Figure 1: Architecture Diagram of Review Methodology

IV. RESULT ANALYSIS

The graph in Figure [2] displays the usage of different research methodologies (Bar Chart).



Figure 2: Distribution of Research Methodologies

The [3] figure demonstrates the main research areas being explored in the field of breast cancer (Pie Chart).

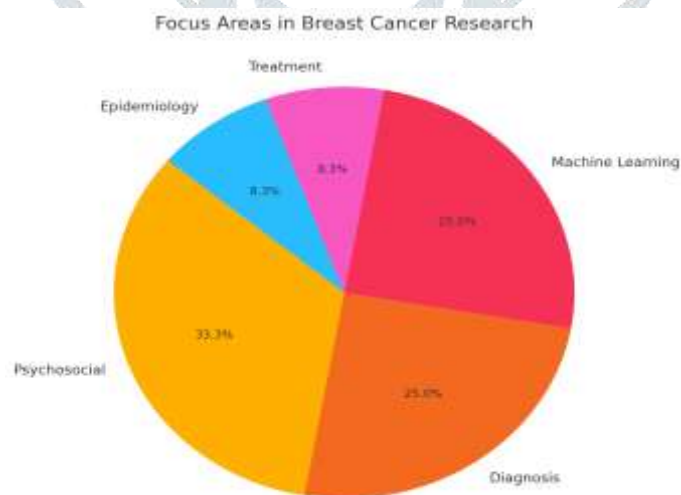


Figure 3: Focus Areas in Breast Cancer Research

The figure [4], a stacked bar chart, displays the research focus and methodology types together (Research Focus vs Methodology Type).



Figure 4: Research Focus vs Methodology Type

Figure [5] shows Heatmap – Methodology vs Focus Area

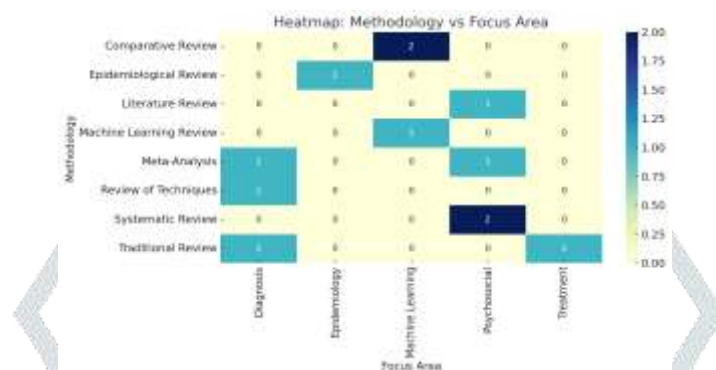


Figure 5: Heatmap – Methodology vs Focus Area

The below image [6] shows the comparative analysis of references vs our work on different aspects

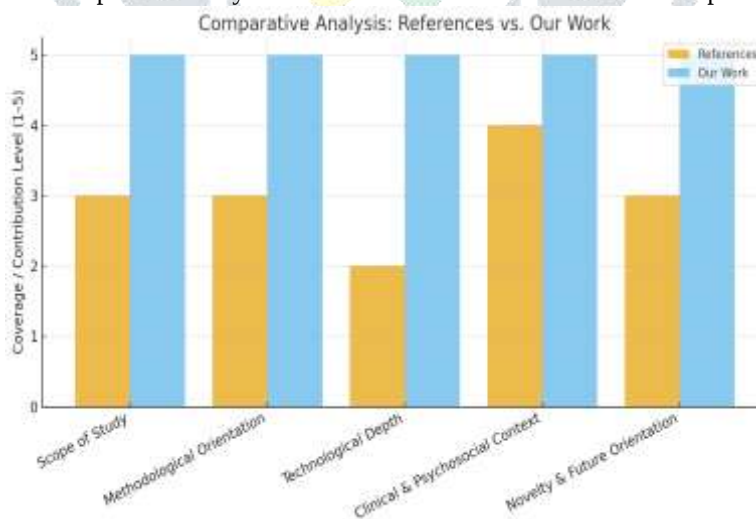


Figure 6. References vs our work

Coverage in the blue polygon (References) is uneven that is, there is a more stringent coverage of clinical/psychosocial compared to methodology, scope, and technology.

The orange polygon (Our Work) creates a balanced full-circle profile, i.e. total integration in the scope, methodology, technology, clinical/psychosocial, and novelty.

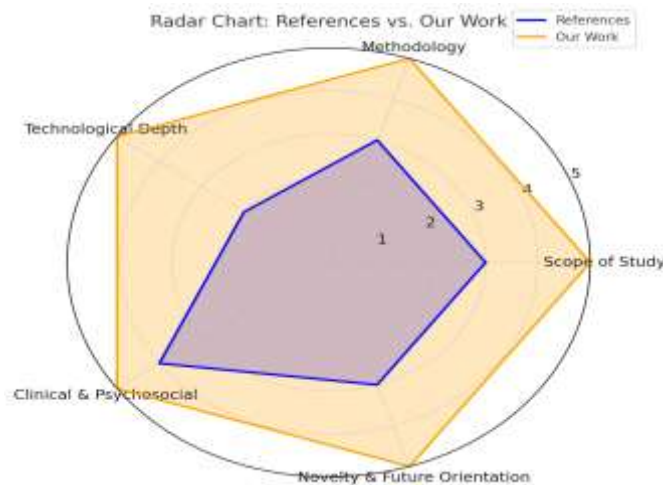


Figure 7. Radar chart references vs. our work

V. CONCLUSION AND FUTURE SCOPE

Although there have been important progresses in detecting, treating and caring for breast cancer, many other ways are still possible to explore and develop further. A main chance for progress is found in connecting artificial intelligence (AI) to various kinds of clinical knowledge such as imaging, disease studies and genetic details, to provide precise and immediate diagnostic support. Machine learning approaches are showing signs of helping, yet wider and more representative datasets and understandable AI models are still needed for them to be used widely by patients and healthcare workers. Evolution in personalized medicine will focus on better ways to study molecules and the immune system, so that treatments can be personalized and unnecessary treatments can be eliminated. Treatment of triple-negative breast cancer is especially focusing on immunotherapy and targeted biological agents. Breast cancer care needs immediate attention for its differences around the world. Screening, early diagnosis and advance treatment are often hard to obtain in economically weak countries. Healthcare frameworks being developed in the future should pay attention to every patient being able to get care, the affordability of technology and care that is culturally appropriate. Also, the psychosocial side of long-term cancer survival deserves more study. Quality of life should be evaluated over time, there should be mental health support available after treatment, counseling for sexual changes and opportunities for people to get back to work should all be included in cancer care. It would also be helpful for future studies to look at the ongoing results for patients such as risks of relapse and other cancers, by using mobile apps, wearable devices and telehealth platforms to let patients monitor their condition on their own.

It brings together major developments and issues in breast cancer research happening in areas such as diagnosis, machine learning, treatment, variations in statistics and aspects of mental health and social life. Using old and current technologies together has changed the worldwide way breast cancer is handled. Studies have documented that standard screening and treatment approaches are highly effective and comparative studies spotlight that machine learning and AI have become important in the fields of radiology and prediction modeling. These kinds of reviews explain the great importance of helping patients with emotional and social support, especially considering survivorship, mental health and life quality. As existing diagnostic and treatment options keep improving, it is still hard to overcome resistance in treatments, problems with overdiagnosis and the gap in healthcare access for many. The results show that continuing innovation, involving different areas of medicine and focusing on the needs of patients helps early discovery, customize treatments and improve the outcomes of patients with breast cancer. In short, connecting advanced studies with real-world breast cancer treatment will remain very important to winning the battle against breast cancer in the future.

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REFERENCES

- [1] Libson, S., and Lippman, M. 2014. A review of clinical aspects of breast cancer. *International Review of Psychiatry*, 26(1): 4–15. <https://doi.org/10.3109/09540261.2013.852971>.
- [2] Waks, A. G., and Winer, E. P. 2019. Breast cancer treatment: a review. *JAMA*, 321(3): 288–300. doi:10.1001/jama.2018.19323.
- [3] Mokhatri-Hesari, P., and Montazeri, A. 2020. Health-related quality of life in breast cancer patients: review of reviews from 2008 to 2018. *Health and Quality of Life Outcomes*, 18: 1–25. <https://doi.org/10.1186/s12955-022-01942-w>.
- [4] Montazeri, A. 2008. Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007. *Journal of Experimental & Clinical Cancer Research*, 27: 1–31. <https://doi.org/10.1186/1756-9966-27-32>.
- [5] Hassan, A. M., and El-Shenawee, M. 2011. Review of electromagnetic techniques for breast cancer detection. *IEEE Reviews in Biomedical Engineering*, 4: 103–118. doi:10.1109/RBME.2011.2169780.
- [6] Sheppard, C. 2007. Breast cancer follow-up: literature review and discussion. *European Journal of Oncology Nursing*, 11(4): 340–347. <https://doi.org/10.1016/j.ejon.2006.09.001>.
- [7] Fatima, N., Liu, L., Hong, S., and Ahmed, H. 2020. Prediction of breast cancer, comparative review of machine learning techniques, and their analysis. *IEEE Access*, 8: 150360–150376. doi:10.1109/ACCESS.2020.3016715.
- [8] Lim, C. C., Devi, K. M., and Ang, E. 2011. Anxiety in women with breast cancer undergoing treatment: a systematic review. *JBIM Evidence Implementation*, 9(3): 215–235. doi:10.1111/j.1744-1609.2011.00221.x.
- [9] Mousavi, S. M., Montazeri, A., Mohagheghi, M. A., Jarrahi, A. M., Harirchi, I., Najafi, M., and Ebrahimi, M. 2007. Breast cancer in Iran: an epidemiological review. *The Breast Journal*, 13(4): 383–391. <https://doi.org/10.1111/j.1524-4741.2007.00446.x>.

- [10] Liberman, M., Sampalis, F., Mulder, D. S., and Sampalis, J. S. 2003. Breast cancer diagnosis by scintimammography: a meta-analysis and review of the literature. *Breast Cancer Research and Treatment*, 80: 115–126. <https://doi.org/10.1023/A:1024417331304>.
- [11] Marla, S., and Stallard, S. 2009. Systematic review of day surgery for breast cancer. *International Journal of Surgery*, 7(4): 318–323. <https://doi.org/10.1016/j.ijsu.2009.04.015>.
- [12] Hong, R., and Xu, B. 2022. Breast cancer: an up-to-date review and future perspectives. *Cancer Communications*, 42(10): 913–936. <https://doi.org/10.1002/cac2.12358>.
- [13] Jansen, L. A., Backstein, R. M., and Brown, M. H. 2014. Breast size and breast cancer: a systematic review. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, 67(12): 1615–1623. <https://doi.org/10.1016/j.bjps.2014.10.001>.
- [14] Puliti, D., Duffy, S. W., Miccinesi, G., De Koning, H., Lynge, E., Zappa, M., and Paci, E. 2012. Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review. *Journal of Medical Screening*, 19(1_suppl): 42–56. <https://doi.org/10.1258/jms.2012.012082>.
- [15] Islam, T., Dahlui, M., Majid, H. A., Nahar, A. M., Mohd Taib, N. A., Su, T. T., and MyBCC Study Group. 2014. Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Public Health*, 14: 1–13. <https://doi.org/10.1186/1471-2458-14-S3-S8>.
- [16] Gardezi, S. J. S., Elazab, A., Lei, B., and Wang, T. 2019. Breast cancer detection and diagnosis using mammographic data: systematic review. *Journal of Medical Internet Research*, 21(7): e14464. doi:10.2196/14464.
- [17] Paraskevi, T. 2012. Quality of life outcomes in patients with breast cancer. *Oncology Reviews*, 6(1): e2. doi:10.4081/oncol.2012.e2.
- [18] Haddou Rahou, B., El Rhazi, K., Ouasmani, F., Nejari, C., Bekkali, R., Montazeri, A., and Mesfioui, A. 2016. Quality of life in Arab women with breast cancer: a review of the literature. *Health and Quality of Life Outcomes*, 14: 1–13. <https://doi.org/10.1186/s12955-016-0468-9>.
- [19] Mourouti, N., Kontogianni, M. D., Papavagelis, C., and Panagiotakos, D. B. 2015. Diet and breast cancer: a systematic review. *International Journal of Food Sciences and Nutrition*, 66(1): 1–42. <https://doi.org/10.3109/09637486.2014.950207>.
- [20] Magai, C., Consedine, N., Neugut, A. I., and Hershman, D. L. 2007. Common psychosocial factors underlying breast cancer screening and breast cancer treatment adherence: a conceptual review and synthesis. *Journal of Women's Health*, 16(1): 11–23. <https://doi.org/10.1089/jwh.2006.0024>.
- [21] Hosni, M., Abnane, I., Idri, A., de Gea, J. M. C., and Alemán, J. L. F. 2019. Reviewing ensemble classification methods in breast cancer. *Computer Methods and Programs in Biomedicine*, 177: 89–112. <https://doi.org/10.1016/j.cmpb.2019.05.019>.
- [22] Zerouaoui, H., and Idri, A. 2021. Reviewing machine learning and image processing based decision-making systems for breast cancer imaging. *Journal of Medical Systems*, 45(1): 8. <https://doi.org/10.1007/s10916-020-01689-1>.
- [23] Marshall, M. B., Moynihan, J. J., Frost, A., and Evans, S. R. T. 1994. Ectopic breast cancer: case report and literature review. *Surgical Oncology*, 3(5): 295–304. [https://doi.org/10.1016/0960-7404\(94\)90032-9](https://doi.org/10.1016/0960-7404(94)90032-9).
- [24] Emilee, G., Ussher, J. M., and Perz, J. 2010. Sexuality after breast cancer: a review. *Maturitas*, 66(4): 397–407. <https://doi.org/10.1016/j.maturitas.2010.03.027>.
- [25] Yassin, N. I., Omran, S., El Houbay, E. M., and Allam, H. 2018. Machine learning techniques for breast cancer computer-aided diagnosis using different image modalities: a systematic review. *Computer Methods and Programs in Biomedicine*, 156: 25–45. <https://doi.org/10.1016/j.cmpb.2017.12.012>.