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Optimizing Breast Cancer Screening Outcomes in Dense Breasts: Diagnostic Performance, Cost-Effectiveness, and Implementation of Supplemental Modalities

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Abstract

Dense breast tissue is a major challenge to screening of breast cancer since it covers about 40-50% of the breast and hides the lesions in traditional mammography. This weakness requires the efficient use of additional imaging modalities for high-risk patients. The following paper is a comparative analysis of the major supplemental imaging techniques, such as ultrasound, Magnetic Resonance Imaging (MRI), Contrast-Enhanced Spectral Mammography (CESM), Digital Breast Tomosynthesis (DBT), and AI-assisted mammography. A literature review was conducted in databases like PubMed, ScienceDirect, and Google Scholar, and peer-reviewed articles published since 2016, and those that concentrated on breast cancer screening in high-density breasts were assessed. The review is a confirmation of the role that mammography plays at its core, but indicates the improved detection of cancer with the help of supplemental ultrasound and MRI. Importantly, CESM has a similar diagnostic potential as MRI and the practical advantages of lower costs and shorter scan time. DBT enhances clear images by reducing overlap between tissues, and it effectively reduces the rate of recollection among patients. Moreover, AI-assisted mammography is one of the essential developments that will raise the detection of cancer in dense breasts and may even prevent the use of auxiliary procedures. The results strongly reflect the need of implementation of tailored and risk-based screening methods where such advanced add-on imaging technologies are combined with Artificial Intelligence, which is likely to elevate screening accuracy, clinical outcomes, affordability, and ultimately make a significant contribution to lowering the rates of mortality of breast cancer.

INDEX TERMS: Breast Density, Breast Cancer Screening, Supplemental Screening Strategies, Breast Cancer Risk, Ultrasound, MRI, CESM, DBT, AI, Risk-Stratified Screening, Diagnostic Performance, Cost-Effectiveness, MRI (AB-MRI)

I. INTRODUCTION

Well-planned screening helps to increase the survival rates of breast cancer. It remains the most widespread type of cancer in women worldwide, and early diagnosis has a considerable impact on the results. One of the determinants that influences the risk of cancer and the accuracy of the screening process is the breast density, or the percentage of fat to fibroglandular tissue that is seen on the mammogram. It is also advised that if women go through mammographic screening annually, the chances of death by breast cancer are minimized by 20 percent [1]. As suggested by previous studies, around 40-50% of women over the age of 40 have dense or heterogeneous breasts, which are further classified as C and D in the Breast Imaging Reporting and Data System (BI-RADS) [2].

The masking effect of highly dense breast tissue can significantly reduce the sensitivity of conventional mammography, hindering early cancer detection [3]. Supplemental modalities, such as contrast-enhanced spectral mammography (CESM), have been investigated. Meta-analyses indicate that CESM provides high specificity and sensitivity in identifying lesions hidden in dense breasts [4]. Magnetic resonance imaging is also one of the most sensitive imaging techniques; a recent study evaluated MRI and found its sensitivity and specificity to be higher than that of mammography [5]. The accuracy, specificity, and recall rate of mammography with supplemental ultrasonography were higher than those of mammography alone [6]. Digital breast tomosynthesis (DBT) offers superior lesion visualization than conventional mammography, as suggested by certain previous studies. However, its advantage for women with highly dense breasts is still unclear [7]. To improve early detection and provide the best individualized treatment, it is necessary to determine the best screening method for women with dense breasts [1].

According to previous studies, millions of women are diagnosed with breast cancer each year. It is also noted that breast cancer continues to be one of the leading causes of female mortality, with hundreds of thousands of them dying from the disease annually [8]. Various

screening guidelines are employed in order to diagnose breast cancer at an early stage. The protocols enhance survival rates during breast cancer patients with dense breast since they provide less invasive treatments [9]. Conventional mammography is still the most common screening approach available because it is easily accessible and can effectively reduce the rate of mortality [10]. It is very insensitive in women who have dense breasts and brings about a high risk of cancer by hiding lesions and abnormalities [11]. Researchers are investigating personalized screening by taking individual risk factors and breast density into account for detecting breast cancer early [12]. Other screening tools, including ultrasound, CESM, MRI, and AI mammography, are being explored because mammography doesn't function well for dense breasts [6, 13]. Physicians get help from these techniques in customizing screening to each woman's unique requirements [1].

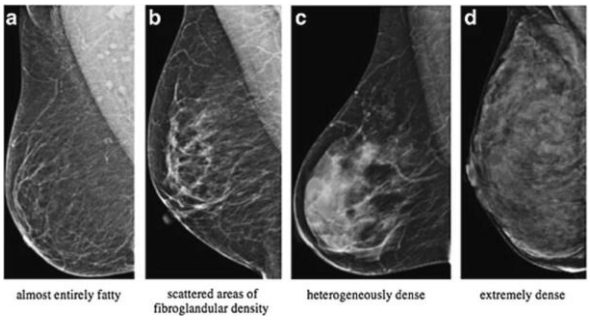

Figure 1: BI-RADS breast density categories shown from low to high density [3].

The proportion of fibroglandular tissue to fatty tissue seen on a mammogram is known as breast density [11]. Breast density is divided into four categories based on the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS): A–almost entirely fatty, B–diffuse fibroglandular, C–heterogeneously dense, and D–extremely dense [14]. Dense breasts (categories C or D) not only make tumors harder to detect on mammography but also increase the breast cancer risk [3]. The phenomenon "masking effect" makes abnormalities harder to detect because both tumors and dense tissue appear white on mammograms. It is common practice to use additional imaging techniques to address the limitations of mammography. Reconstructions of three-dimensional images used in digital breast tomosynthesis can improve lesion visibility and reduce recall rates [7]. In terms of diagnostic accuracy comparable to that of MRI, Contrast-Enhanced Spectral Mammography (CESM) allows vascular assessment of lesions by combining low- and high-energy imaging [4]. Ultrasound (US) is a safe imaging method because it does not use radiation and can detect tumors in women with dense breasts that mammography might miss, despite being dependent on the operator's skill [15]. Magnetic resonance imaging (MRI), because of its high cost and restricted availability, is still the most sensitive method for detecting breast cancer, especially in women who are at high risk [5]. Sensitivity indicates how well the test detects women who actually have the disease, while specificity refers to how well the test detects women who do not have the disease. High specificity minimizes false positives and unnecessary follow-ups, while high sensitivity allows for early identification, particularly in women with dense breasts. Such definitions align with previous research assessing breast density, cancer risk, and screening performance [4].

Supplemental imaging techniques (MRI, CESM, DBT, and ultrasound) have been independently evaluated for breast screening in women with high breast density. During the past few years, several large-scale trials and systematic reviews have shown improvements in detection rates over mammography alone [13]. Studies indicate that in many dense-breast cases, contrast-enhanced spectral mammography (CESM) can achieve sensitivity similar to MRI; its specificity and cost vary significantly among healthcare settings [16]. In breasts

Table 1. PICOS framework for inclusion and exclusion criteria

Component	Inclusion Criteria	Exclusion Criteria
Population (P)	Women with heterogeneously or extremely dense breast tissue and negative mammography results	Studies involving non-dense breasts, male patients, or non-human studies
Intervention/Exposure (I)	Use of supplemental imaging techniques, such as contrast-enhanced spectral mammography (CESM), digital breast tomosynthesis (DBT), magnetic resonance imaging (MRI), and ultrasound (US)	Studies limited to standard 2D mammography
Comparison (C)	Compared with standard 2D mammography or between different supplemental techniques	Studies without a reference standard
Outcomes (O)	Diagnostic performance matrices that are reported include cost-effectiveness, sensitivity, specificity, recall rate, PPV, and cancer detection rate (CDR)	Studies lacking diagnostic outcomes
Study Design (S)	Prospective or large retrospective cohort studies, cross-sectional studies, and meta-analyses of diagnostic accuracy (2016-2025)	Single-case reports, editorials, and small-sample studies
Other Criteria	Peer-reviewed English publications between 2016 and 2025	Non-peer-reviewed publications in other languages or before 2016

with different densities, digital breast tomosynthesis (DBT) has been shown to reduce recall rates and enhance lesion visibility; however, the further advantage for highly dense tissue is still less certain [7]. AI-assisted mammography can also be used to eliminate the need for additional mammography, with sensitivity and specificity comparable to those of supplemental ultrasound. Furthermore, these advancements from standard screening methods to personalized techniques mainly focus on the early detection and prevention of breast cancer [6]. Recent studies also show that using several screening modalities without specific guidelines for when and how often to apply those increases the number of false positives and incorrect diagnoses [6]. Few studies have comprehensively evaluated key supplemental imaging modalities across different settings and dense-breast populations to establish an optimal balance between their benefits and risks [17]. The absence of comprehensive long-term outcome data, including interval cancer incidence, stage at diagnosis, and mortality, limits understanding of its real-world impact [2]. Furthermore, many proposals may not be practical worldwide because the limited resources of low- and middle-income regions were not properly taken into consideration [12]. To incorporate the most recent studies, compare diagnostic performance, analyze risks, and assess feasibility across settings for women with dense breasts, a thorough synthesis is necessary. This review assesses the diagnostic efficiency and cost-effectiveness of supplemental screening modalities, including digital breast tomosynthesis (DBT), ultrasound (US), magnetic resonance imaging (MRI), contrast-enhanced spectral mammography (CESM), and AI in women with dense breasts and negative mammogram reports from previous studies. It also looks for research gaps to provide risk-based ideal screening methods.

Research Questions (RQs):

RQ1: What are the current challenges in breast density assessment?

RQ2: How do supplemental imaging modalities compare in detecting breast cancer in dense breasts?

RQ3: In what ways do several imaging modalities affect diagnostic performance?

II. METHODOLOGY

The central focus of this review was on systematically examining supplemental screening techniques for women with an elevated risk of breast cancer who have dense breast tissue. In accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) principles, the review was conducted, however, no quantitative synthesis was performed, and the review was not registered prospectively in PROSPERO. Further, a transparent and organized methodology was applied to ensure integrity throughout the review process.

A. Search Strategy

Information Sources: A comprehensive search was conducted to identify recent papers and relevant studies published between August 2016 and July 2025. PubMed, PubMed Central (PMC), ScienceDirect, and Google Scholar from widely accessible digital libraries were used. Specialized databases such as Embase and Cochrane were not part of the search strategy due to a lack of access and resource limitations. All search decisions and limitations were explicitly documented to maintain transparency.

Search Query: To identify up-to-date research, a comprehensive search was carried out by exploring selected databases. Medical Subject Headings (MeSH) and keyword terms such as “dense breasts”, “supplemental imaging techniques”, “contrast-enhanced spectral mammography”, “digital breast tomosynthesis”, ultrasound”, “magnetic resonance imaging”, and artificial intelligence” were used in the search strategy.

Boolean operators AND, OR, and NOT were used to narrow down the search results. This combination aided in the screening of human subject-focused research for high-risk women with dense breasts. The search method utilized the following aspects of a structured Boolean expression: (“dense breast” OR “breast density”) AND (“breast cancer screening” OR “screening mammography”) AND (“ultrasound” OR “magnetic resonance imaging” OR “MRI” OR “digital breast tomosynthesis” OR “contrast-enhanced spectral mammography” OR “CESM”) NOT (“animal” OR “case report”).

Other Search Methods: To ensure comprehensiveness, backward and forward snowballing were employed to review the reference lists of the included publications and related reviews. This review does not include grey literature, such as abstract-only research, conference proceedings, and other non-peer-reviewed data.

B. Eligibility (Inclusion/Exclusion) Criteria:

In accordance with the population, intervention, comparison, outcomes, and study design (PICOS framework), which is outlined in this table, articles were screened using specified inclusion and exclusion criteria:

C. Study Selection Process:

The selection of the study complied with the transparency and reproducibility requirements of the PRISMA guidelines. EndNote software was used to import references from PubMed, Google Scholar, ScienceDirect, and PMC for reference management and to prevent duplication. In the studies, screening was conducted in two stages. In the first step, all titles and abstracts were reviewed by two independent reviewers using PICOS-based eligibility criteria. When any differences could not be resolved through discussion, a third reviewer was brought in to make the final decision. A second round of review was conducted by the same reviewers who independently examined the full texts of all possibly qualifying articles. At the full-text stage, reasons for exclusion were carefully noted. To maintain uniformity and transparency, both stages were screened using the same criteria. In the final synthesis, only studies that met all inclusion criteria after reviewer agreement were included.

PRISMA flow diagrams were created to describe the process of identifying, screening, determining eligibility, and including participants. Using database searches and supplementary sources, 100 records were discovered, of which 90 were found through database searches and 10 by searching supplementary sources. There were only 30 records left for title and abstract screening after the duplicates were removed. As a result of this stage, 70 records were excluded because they did not meet the eligibility requirements. In total, 22 full-text publications were reviewed. Among these publications, 8 were removed due to insufficient methodological relevance or the absence of the complete text. There were 22 papers that met all criteria for inclusion in the final qualitative synthesis. As shown in Figure 2, the PRISMA flow diagram provides a visual representation of the numerical breakdown of each stage in order to ensure methodological transparency and reproducibility.

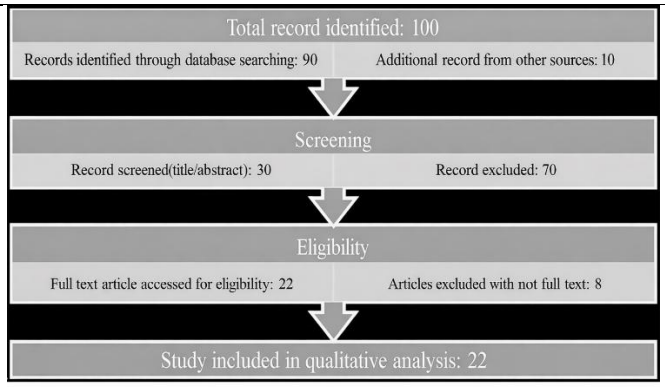

Figure 2: PRISMA flow diagram for study selection

The 22 included papers consist of 10 reviews or expert guidelines published between 2016 and 2025, 9 cohort studies published between 2016 and 2024, and 6 systematic reviews/meta-analyses published between

Table 2. Summary of included studies and their characteristics

Study Design	Number of Studies	Publication Years	References
Systematic Reviews / Meta-analyses	6	2021–2024	[2], [4], [7], [13], [16], [17]
Cohort Studies	7	2016–2024	[6], [11], [12], [14], [15], [19]-[22]
Reviews / Expert Guidelines	10	2016–2025	[1], [3], [5], [8], [9], [10], [18]
Total / Overall	22	2016–2025	[1]–[22]

Table 3. Summary of risk-of-bias assessment of the included studies.

Ref No.	Author Name	Study Design	Tool Used	Overall Risk of Bias
[1]	Mann et al.	Recommendation/Expert Guidelines	QUADAS-2	Moderate
[2]	Mokhtary et al.	Systematic Review & Meta-analysis	CASP	High
[3]	Nissan et al.	Narrative Review	CASP	Moderate
[4]	Liu et al.	Systematic Review & Meta-analysis	CASP	Low
[5]	Sitges et al.	Narrative Review	CASP	Moderate
[6]	Lee et al.	Retrospective Study	NIH	High
[7]	Raichand et al.	Systematic Review	CASP	Moderate
[8]	Bray et al.	Descriptive Epidemiological Study	QUADAS-2	Low
[9]	Marmot et al.	Independent Review	QUADAS-2	Moderate
[10]	Tomlinson-Hansen et al.	Narrative Review	NIH	High
[11]	Boyd et al.	Observational Cohort	NIH	Moderate
[12]	Bertsimas et al.	Cohort Observational Study	NIH	High
[13]	Abu Abeelh et al.	Systematic Review	CASP	High
[14]	Kim et al.	Cohort Study	NIH	Moderate
[15]	Vourtsis et al.	Cohort Observational Study	NIH	Low
[16]	Daniaux et al.	Systematic Review	CASP	Moderate
[17]	Tran et al.	Meta-analysis	CASP	Low
[18]	USPSTF et al.	Clinical practice guideline (USPSTF recommendation).	QUADAS-2	Moderate
[19]	Tan et al.	Retrospective observational study	NIH	Moderate
[20]	Mansour et al.	Retrospective observational study	CASP	High
[21]	Shermis et al.	Cohort Study	NIH	High
[22]	Richman et al.	Observational study	NIH	Moderate

2021 and 2024. Overall, the studies included a wide spectrum of evidence, from primary research to expert opinions. Table 2 describes a summary of the study's design, number of studies, years of publication, and references:

D. Data Extraction and Data Items

A structured Excel sheet was used to collect data from selected studies. It was mainly employed to accurately analyze the studies, ensuring accuracy, consistency, and comparability of the diagnostic performance of different supplemental modalities. The primary findings and limitations of these modalities were also recorded. A narrative synthesis was used to compare and summarize the diagnostic accuracy of different imaging techniques in an organized way. The data extraction strategy and synthesis protocols were used to accurately compare positive predictive value (PPV), recall rate, sensitivity, specificity, and cancer detection rate (CDR) from the available studies.

E. Risk of Bias (Quality) Assessment

This review carefully evaluated all included studies using different tools to assess their quality. The tools used included the QUADAS-2 tool, the CASP checklist, and the NIH Quality Assessment Tool were used to examine diagnostic accuracy studies, systematic reviews and meta-analyses, and observational studies, respectively. These tools were also used to evaluate methodological quality and possible risk of bias. After evaluation, all studies were categorized as having a low, moderate, or high risk of bias to guide the overall discussion. These ratings were then used to give greater importance to studies with stronger and more trustworthy methodologies. Table 3 summarizes the methodological characteristics of the included studies.

III. RESULTS

A. Synthesis of Results

The synthesis of results focuses on key aspects of breast screening in women with dense breast tissue. It further summarizes the results from 22 studies included in the review. Dense breasts not only increase the risk of breast cancer but also make it more difficult for mammography to detect abnormalities. MRI and CESM demonstrate the highest sensitivity among the imaging modalities assessed, whereas ultrasound and AI-assisted imaging provide supplementary support for identifying lesions that mammography might miss. Patient knowledge, medical recommendations, and accessibility substantially influence adherence. By combining multimodal screening methods, early detection may be enhanced, and the long-term outcome may be improved, permitting less aggressive treatment and reducing overall health-care costs. The diagnostic performance of several modalities was compared using a narrative synthesis. The following metrics are reported: sensitivity, specificity, positive predictive value (PPV), and cancer detection rate (CDR). Qualitative findings were supplied in cases where quantitative data were not available. As shown in Table 3, the narrative synthesis of diagnostic performance in different modalities was summarized.

Previous studies consistently identify several key challenges for the accurate assessment of breast density. Due to its ability to obscure lesions, increase false-negative results, and complicate early cancer detection, dense fibroglandular tissue lowers mammographic sensitivity [1], [11]. Variations in imaging methods and subjective interpretation of BI-RADS classification also affect breast density evaluation, resulting in uneven categorization among readers and institutions [6], [20]. Furthermore, single-point measures are not accurate for long-term risk assessment because breast density varies with age and hormonal factors [2], [14]. Volumetric and AI-based approaches still need to be validated before being used in clinical settings, considering their potential to standardize evaluation [19], [20].

Efficacy of Supplemental Screening Modalities:

A previous study showed that women who have very dense breasts need to have additional screening since they are likely to develop breast cancer and have lower mammography sensitivity. In women who are premenopausal or whose breast density changes quickly, mammography alone may miss malignancies in dense tissue [1], [2]. Combining ultrasound with mammography as an additional imaging modality increases detection rates, particularly for small and node-negative cancers [6]. Several studies suggests that breast MRI monitoring at longer intervals may be beneficial for women with thicker breasts, although the ideal frequency is still being researched [1]. Contrast-enhanced spectral mammography (CESM) offers high sensitivity and specificity and detects problems that traditional mammography may miss [4]. Digital breast tomosynthesis (DBT) increases the early detection rates of cancers in dense breast tissue. In contrast to conventional mammography, it also decreases recall rates [7]. AI-assisted imaging can be used in conjunction with 3D automated breast ultrasonography. It also reduces false negatives and increases early detection by enhancing mammographic analysis [19]. A woman with dense breasts who undergoes mammography sometimes shows a negative mammogram. To improve visibility and detection accuracy, molecular breast imaging provides a useful answer to the clinical problems of detecting cancer [21]. Personalized screening methods, which are designed around each patient's particular risk profile and tissue characteristics, are supported by previous studies. These methods aim to detect minor alterations sooner and provide more focused recommendations [12].

Predictors of Adherence to Screening Protocols:

Healthcare professionals provide essential recommendations that include practical considerations such as accessibility, cost, and insurance coverage. These factors also play a key role in determining a patient's involvement in supplemental imaging [13]. When women clearly understand the risks of dense breasts and the limitations of mammography in hiding

Table 3: A narrative synthesis of the diagnostic efficacy of screening methods for breast cancer in women with dense breasts

Screening Modalities	Sensitivity	Specificity	Cancer Detection Rate (CDR)	Positive Predictive Value (PPV)	References
2D Mammography	Sensitivity is lower due to dense tissue masking	Moderate specificity	CDR is lower in dense breasts	PPV is lower due to missed cancers	[8], [9], [11]
Digital Breast Tomosynthesis (DBT)	Improved sensitivity compared to 2D mammography	Slightly higher Specificity than 2D mammography	A moderate increase in CDR is observed	Improved PPV with reduced recall rates	[7], [22]
Ultrasound (HHUS/ABUS)	High sensitivity	Variable specificity	Improved CDR rate when combined with mammography	Moderate PPV; may decrease with increased false positives	[6], [15], [19]
Magnetic Resonance Imaging (MRI)	Higher sensitivity than other screening modalities (>90%)	Moderate specificity, approximately (70–85%)	Highest CDR among all modalities	High PPV, especially for invasive cancers	[1], [5], [13]
Contrast-Enhanced Spectral Mammography (CESM)	High sensitivity, approximately (85–90%)	Moderate specificity, approximately (75–85%)	CDR is Comparable to that of MRI; higher than 2D mammography	Moderate to high PPV	[3], [4], [16]
Molecular Breast Imaging (MBI)	High sensitivity, approximately (80%)	Moderate specificity, approximately (80–85%)	Detects additional cancers missed by mammography	Comparable to ultrasound; moderate PPV	[21]
AI-Based Multimodal Systems	High sensitivity, approximately (85%)	Maintains or slightly improves specificity	CDR improvement when integrated with mammography or ultrasound	Improved PPV by reducing missed lesions	[6], [19], [20]

most of the lesions, they are more likely to participate in supplemental screening programs other than mammography [3]. Public awareness campaigns and follow-up programs are organized. They have been effective in encouraging people's long-term adherence to recommended screening protocols [5].

Long-Term Outcomes and Cost-Effectiveness:

The cost-effectiveness in this section is discussed in a theoretical manner, because no quantitative economic study (ICER/QALY) has been performed. Supplemental screening techniques, especially MRI, CESM, and ultrasound, allow for early detection and can help reduce death rates when compared to mammography alone [1], [4]. Due to the higher initial costs of MRI and CESM, a problem arises that further necessitates the personalized, risk-based screening methods combining mammography, ultrasound, and AI-assisted imaging, which are cost-effective and reduce the incidence of interval cancers and long-term treatment expenses [12], [17], [19]. Using several methods further improves patient outcomes through early detection. It may reduce the need for aggressive therapies and allow for less invasive procedures, such as breast-conserving surgery rather than mastectomy [5], [16]. To maximize healthcare by improving diagnostic accuracy and reducing needless treatment and follow-ups is ensured by multimodal imaging tailored to each patient's risk profile, which maximizes diagnostic accuracy and minimizes needless treatment and follow-ups [7], [21]. Continuous adherence to supplemental screening is necessary for achieving such therapeutic advantages since non-compliance can compromise the ability of these strategies in lowering mortality and medical expenses [18].

B. Risk of Bias within Studies

The majority of the 22 studies were rated as being of moderate to high quality and made up the basis of this review. The high-quality studies with strong methodological rigor were systematic reviews and meta-analyses as demonstrated by thorough literature searches and consistent reporting of their findings [2], [4], [7], [13], [17]. Most cohort studies were prospective and had explicit inclusion criteria. However, several had small sample numbers or insufficient follow-up data [6], [14]-[16], [19], [21], [22]. Although reviews and expert suggestions were comprehensive, they were sometimes constrained by unclear search methodologies and varied

Table 4: Comparison of key studies that assessed various methods for screening for breast cancer in women with dense breasts.

Study (Ref.)	Population/ Setting	Modality/ Intervention	Main Findings	Strengths	Limitations
Liu J et al. [4]	Women getting their breast evaluation	Contrast-Enhanced Spectral Mammography (CESM)	CESM demonstrates good sensitivity and specificity comparable to MRI.	Large data pool; efficient meta-analysis.	Varying protocols; possible bias.
Sitges C & Mann RM [5]	Extremely dense breasts in women	Breast Magnetic Resonance Imaging (MRI) screening	MRI increased cancer detection with a moderate recall rate.	Concentrated on the dense-breast group; updated data.	High cost; limited availability.
Lee SE et al. [6]	Women with dense breasts	Mammography vs. Artificial Intelligence vs. Ultrasound	AI and US enhanced detection over mammography; AI accuracy was comparable to that of radiologists.	Direct tools comparison: practical significance.	Retrospective; small sample.
Raichand S et al. [7]	Dense-breast women with added risk factors	Digital Breast Tomosynthesis (DBT)	Comparing DBT to 2D mammography, the first method increased detection but reduced recalls.	Extensive review; multiple populations included.	No long-term outcomes.
Abu Abeelh E & AbuAbeileh Z [13]	Women with dense breast tissue	Mammography, Ultrasound, MRI	MRI was the most sensitive, followed by US and mammography	Clear comparative synthesis.	Few studies; varied methods.
Daniaux M et al. [16]	Newly diagnosed breast cancer patients	Contrast-enhanced Spectral Mammography(CESM) vs Mammography, US, MRI	CESM accuracy is similar to MRI and more accurate than US or mammography	Detailed multimodal comparison.	Focused on staging, not screening.
Tran E & Ray K [17]	Dense-breast women with negative mammograms	Meta-analysis of MRI, US, MBI	MRI works best; US and MBI have limited value.	Dense-breast subgroup; pooled analysis.	Study heterogeneity; no mortality data.
Shermis RB et al. [21]	Dense-breast women with negative mammography	Molecular Breast Imaging (MBI)	MBI detected ~7.7 extra cancers/1,000; recall 8.4%.	Real-world clinical data.	Retrospective: radiation exposure.

study populations [1], [3], [5], [8], [12], [18], [20]. Common methodological limitations in all of the included studies were variability in breast density classification, study population heterogeneity, variations in imaging procedures, and limited sample sizes in certain cohort studies.

IV. DISCUSSION

A. Summary of Evidence

This review evaluated breast cancer screening techniques for women with dense breast tissue. This study combined data from 22 studies. Mammographic breast density was consistently found to be a significant limitation of mammography due to its lower sensitivity and a strong independent risk factor for breast cancer across all studies [1], [11], [14]. In comparison to mammography alone, other imaging modalities, including digital breast tomosynthesis (DBT), contrast-enhanced spectral mammography (CESM), magnetic resonance imaging (MRI), ultrasound (US), molecular breast imaging (MBI), and artificial intelligence AI-assisted tools, showed better detection rates in dense breasts [4]-[7], [13], [16], [17], [21]. The highest sensitivity was obtained by MRI and CESM, with MRI exhibiting better lesion characterization and CESM emerging as a viable substitute in situations

Table 5: Comparative summary of cost and accessibility of breast cancer screening modalities in women with dense breasts.

Modality	Cost / Accessibility	Key References
2D Mammography	Lowest cost and most widely available modality; it forms the foundation of national screening programs worldwide.	[1], [18]
Digital Breast Tomosynthesis (DBT)	Moderately higher cost than 2D but increasingly available; compatible with existing mammography systems and feasible for large-scale screening.	[7]
Ultrasound (HHUS / ABUS)	Low to moderate cost; handheld ultrasound is widely available but operator-dependent, while automated systems improve standardization but require dedicated equipment.	[13]
Contrast-Enhanced Spectral Mammography (CESM)	Moderate cost; more affordable and accessible than MRI, requiring IV contrast but using standard mammography infrastructure.	[4]
MRI	Highest cost and limited accessibility; requires advanced equipment, longer examination time, and specialized interpretation—best suited for high-risk women.	[5]
AI-Assisted Imaging	Implementation cost remains variable, but integration improves efficiency and workflow. Accessibility is expanding with digital infrastructure and validation studies.	[6], [19]

where MRI availability or cost is a barrier [4], [5], [16]. Particularly in moderate-density categories, DBT and ultrasound offered progressive cancer detection [6], [7], [15]. Diagnostic accuracy was improved and false positives were decreased with the use of AI and multimodal techniques that integrated mammography with US or digital Breast Tomosynthesis [19], [20]. Overall, the results were consistent with previous studies and new worldwide screening guidelines that emphasize multimodal and risk-stratified screening for women with dense breasts [1], [18].

B. Interpretation of Findings

The risk of developing breast cancer is increased by dense breast tissue, which also makes it more difficult to spot anomalies on a mammogram. It highlights the limitations of using mammography alone [2], [3], [11]. There is increasing evidence that a more individualized strategy, taking into account variables such as personal risk factors, age, and breast density, may improve screening outcomes [12], [18]. For women with very dense breast or at high risk, MRI is the method of choice consistently demonstrates the highest cancer detection rate and the lowest interval cancer rate among all imaging techniques. Different modalities, such as mammography, ultrasound, and AI-assisted approaches, are often assessed according to how well they meet their standards. Nevertheless, there are a few drawbacks to MRI: long periods of examination, claustrophobia, and discomfort from intravenous contrast can all lower patient compliance and result in insufficient or misleading tests. Therefore, timely access to performing an MRI is difficult due to these limitations [5], [6], [17]. Contrast-enhanced spectral mammography (CESM) requires less time for examination and offers sensitivity similar to MRI. Studies have shown that CESM performs effectively, with similar specificity to conventional mammography. As a more practical alternative to MRI, CESM has drawn interest. Therefore, it is also preferred in environments where access to emerging screening techniques is restricted. The availability of appropriate tools and contrast agents affects its value. Additionally, CESM can detect a variety of breast malignancies and has shown a higher true-positive rate in some clinical settings. Therefore, it also lessens the need for follow-up ultrasound tests [4], [16].

Previous studies suggest that MRI has some limitations, although it remains the most accurate imaging method. Its use is influenced by elevated cost, extended scan time, and limited availability [5]. Supplemental ultrasound, especially Automated Breast Ultrasound (ABUS), increases the detection of cancer in dense breasts. However, it is still operator-dependent and has a higher false-positive rate, which has been reported in some studies to be between 4% and 10%. This can result in higher recall rates and needless biopsies. It is nevertheless an appropriate and accessible choice in environments with minimal resources despite these disadvantages [13], [15]. When paired with AI interpretation, DBT improved detection by showing greater lesion visibility and fewer overlapping tissue effects than 2D mammography [6], [7], [19]. As shown in Table 5, a comparative overview of cost and accessibility among breast cancer screening modalities for women with dense breasts is summarized. While MRI offers the highest sensitivity, but limited accessibility and a higher cost [5]. Mammography and ultrasound remain the most practical and affordable screening tools worldwide [1], [13], [18]. Emerging AI-assisted systems are showing potential to enhance efficiency and access in clinical practice [6], [19].

The cancer detection rate (CDR) of digital breast tomosynthesis (DBT) was higher than that of 2-D digital mammography in women with BI-RADS C/D (dense) breasts, with reported values of 5.3 and 3.7 per 1,000 screenings, respectively. In dense breast tissue, a previous study suggests that DBT has a significant additional advantage in enhancing lesion diagnosis [22]. There is potential for improving the interpretation of supplementary breast imaging with the use of artificial intelligence (AI). Automated 3D breast ultrasound (ABUS) and mammography using AI increased

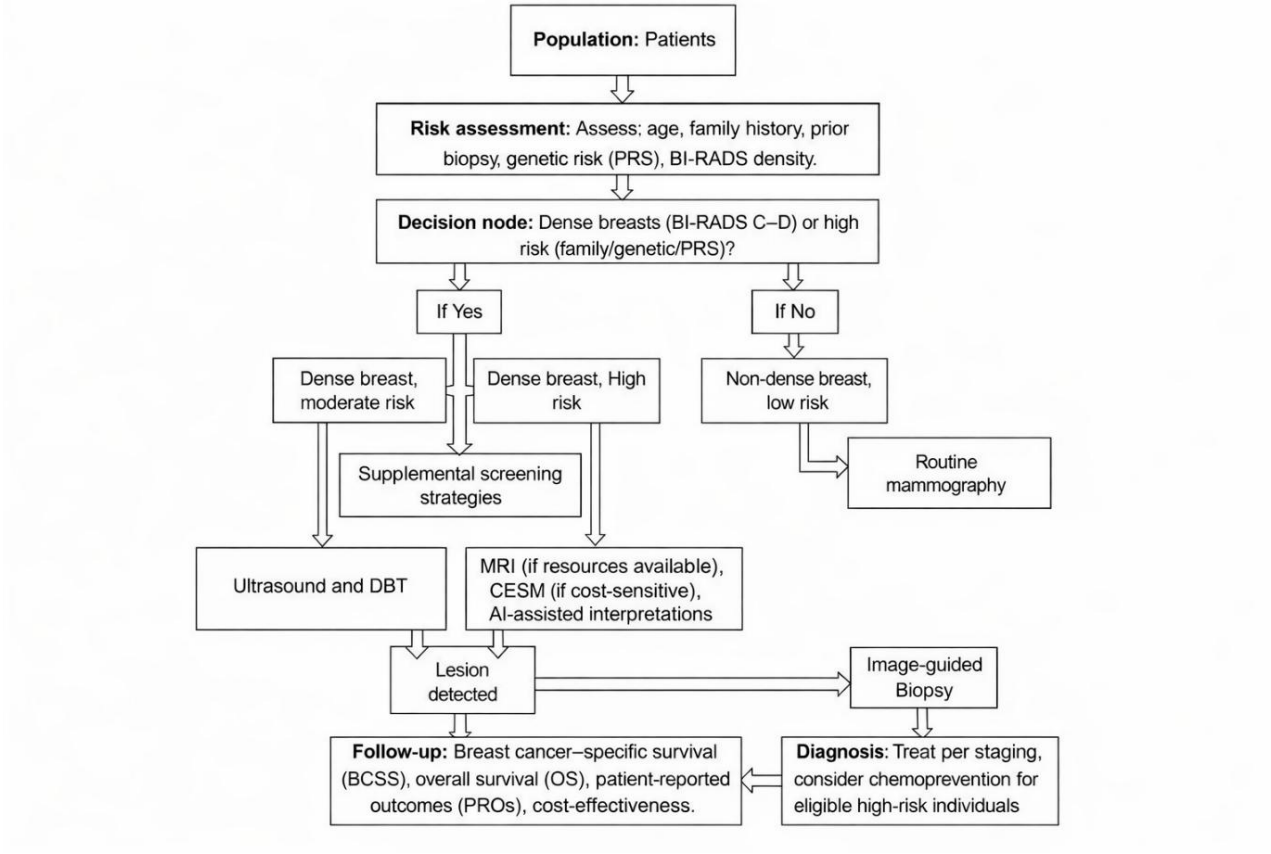

Figure 3: Conceptual algorithm for breast cancer screening [1], [3], [6], [17].

diagnostic efficiency and accuracy in women with dense breasts, confirming its capacity to decrease observer error and reading time [19]. While comparing traditional 2D mammography with DBT and CESM, the latter two provide comparatively greater radiation doses. Nevertheless, the increase stays within globally recognized safety and diagnostic reference ranges. CESM uses two sets of X-ray images at low and high energy levels, so its dual-energy imaging method is responsible for the higher exposure. However, DBT uses slightly higher doses, which come from obtaining multiple projections to construct 3D images [4], [7], [16]. Individual risk should be taken into consideration when developing screening strategies for women with dense breasts. Ultrasonography, digital breast tomosynthesis, and contrast-enhanced spectral mammography are more effective screening techniques for improving early detection in women with heterogeneously dense breast tissue (BI-RADS C) [7], [13]. On the other hand, MRI and CESM are recommended for high-risk women with highly dense breasts (BI-RADS D). MRI is more appropriate because of its higher sensitivity, but if it is not available, CESM serves as an alternative [1], [16]. AI-assisted image interpretation has been demonstrated in studies to enhance lesion characterization. It also normalizes reporting and reduces reader variability, especially in dense breast screening [19], [20]. The Cancer Detection Rate (CDR), defined as the number of malignancies found in every 1,000 women examined, is standardized as the primary measure of screening effectiveness to ensure comparability between modalities for assessing how well imaging modalities operate in practice. Especially in women with dense breasts, this parameter is seen to be clinically more significant than sensitivity alone. The most recent EUSOBI and USPSTF recommendations support individualized screening for women with extremely dense breasts [1], [17], [18]. Because overlapping tissue may conceal lesions in women with dense breasts, the False Negative Rate (FNR) shows malignancies that were not detected during screening. Mammogram sensitivity can drop by as much as 48% in very dense breasts; according to EUSOBI recommendations, almost half of malignancies remain undetected. As noted, MRI, CESM, and ultrasound enhance detection in dense tissue, whereas mammography is less successful in this part of the body. In this high-risk category, lowering the FNR and ensuring early cancer identification are therefore the main objectives of supplemental screening [1], [13].

Worldwide, there are different screening guidelines for women with dense breasts. Routine supplemental screening, such as MRI or ultrasound, is not supported by enough evidence, according to the U.S. Preventive Services Task Force. According to the European Society of Breast Imaging (EUSOBI), breast MRI should be made available to women with extremely dense breasts. Further, studies have demonstrated that the diagnostic performance of supplemental modalities varies. Underscoring the need for a single international standard to support uniform risk assessment and equitable screening procedures around the world [1], [7], [13], [18]. As shown in Figure 3, a conceptual algorithm diagram describes a strategy of screening for breast cancer based on density and risk. BI-RADS density risks are used to

stratify patients, which helps determine which additional modalities, such as MRI, CESM, DBT, ultrasound, or AI-assisted interpretations, should be used. According to previous studies, this strategy prioritizes personalized screening to maximize early detection and resource use [1], [3], [5], [6], [13], [16]-[19], [22].

C. Limitations of the Review

There are some limitations in the review. Only English-language studies from large databases were considered, which may have excluded gray literature and introduced potential publication bias. Methodological heterogeneity among studies, including variations in imaging techniques, sample numbers, and reference standards, creates challenges for meta-analysis and limits direct comparison. The homogeneity of synthesis is impacted by inconsistent inclusion and exclusion criteria in studies. The generalizability of several studies was limited by small sample sizes and single-center data.

D. Limitations of the Available Evidence

Major limitations also exist within the currently available body of evidence. Numerous studies had varying study quality, limited sample sizes, and were retrospective and single-centered [4], [6], [7], [13], [15]. The evaluation of interval cancers and long-term results was limited by short follow-up periods [16], [17]. Additionally, cross-study comparisons were restricted by uneven breast density classification and a lack of uniform BI-RADS reporting [3], [11]. Furthermore, there is still a lack of cost-effectiveness data for supplementary modalities such as MRI, CESM, and MBI, and AI systems need thorough external evaluation before clinical integration [19], [20]. Furthermore, because the majority of research was carried out in North America or Europe, generalizability is limited by the underrepresentation of other populations [1], [7], [18].

E. Implications and Future Directions

For Research: Two critical research gaps include supporting the cost-effectiveness and diagnostic precision of abbreviated MRI (AB-MRI) for women with dense breasts, and the other is addressing AI implementation challenges, such as infrastructure, training, and expense, to facilitate equitable integration across healthcare systems. The current gold standard, MRI, should be compared with modern modalities, such as DBT, CESM, and AI-assisted screening, in large-scale, multicenter trials in the future to guide implementation in various clinical settings [4]-[6], [19]. Researchers need to adopt standardized imaging strategies across breast cancer screening studies to strengthen the methodological rigor and achieve more precise outcomes. In addition to the BI-RADS classification, the use of these strategies makes it easier to compare studies in a meaningful way [3], [6], [7], [13]. In order to determine safer and more efficient pathways, future research should also compare the complication rates of different imaging modalities. Furthermore, it should assess the possible risks associated with different biopsy techniques, such as core needle versus vacuum-assisted procedures [13], [16]. Future studies should also examine long-term outcomes, such as mortality, interval cancer rates, overall survival (OS), and breast cancer–specific survival (BCSS) [17]. Simultaneously, screening procedures should be designed with patient-centered aspects, like comfort, anxiety, and time commitment, in consideration [1], [10]. Furthermore, AI-driven screening models also need to be evaluated on a variety of populations in order to eliminate algorithmic bias and guarantee dependability [12], [19], [20].

For Practice/Policy: The USPSTF and EUSOBI guidelines recommend that clinicians adopt multimodal and personalized screening methods for women with dense breasts. State-level laws in the United States (US) regulating breast density reporting emphasize the value of individualized screening by promoting equity and early detection. The absence of established payment systems is one of the main obstacles to obtaining advanced modalities such as MRI, CESM, and DBT. These technologies remain unaffordable without financial assistance. Therefore, in order to guarantee equal access and encourage the regular utilization of clinically established screening procedures, government authorities must implement appropriate payment systems [1], [6], [7], [18]. Future research should work on the development of safer alternatives, such as gadolinium-free MRI agents and low-iodine CESM agents, to reduce toxicity [4], [5]. Personalized imaging recommendations based on genetic risk profile are becoming more and more important in the advancement of breast cancer screening. Future studies should work on well-known predictive models, like Tyrer-Cuzick or Gail. Tools like the polygenic risk score provide a pathway to more customized screening techniques. In order to promote early detection, these methods guarantee that screening protocols with genetic risk factors enhance the efficiency of resource utilization [1], [4], [6], [12]. Future research should standardize the practical implementation of abbreviated magnetic resonance imaging (AB-MRI) for women who are at high risk of cancer. Recent studies suggest that AB-MRI can provide benefits to large-scale screening programs by significantly reducing scan times while preserving excellent sensitivity [5], [6]. Healthcare providers have the responsibility to clearly describe the challenges so that women who are at high risk can choose the best possible option for themselves without anxiety. Proper planning can adjust screening techniques to the available resources; for example, in low-resource settings, ultrasound and digital breast tomosynthesis (DBT) may be less expensive alternatives to conventional mammography [1], [6], [7]. While remaining practically feasible, the integration of contrast-enhanced spectral mammography (CESM) could improve detection capabilities for middle-resource systems [16]. Future frameworks for screening should also combine high-risk identification with preventive measures such as chemoprevention, which can be applied using validated risk models when clinically appropriate [12], [18]. As recommended by EUSOBI and USPSTF, high-resource settings should include MRI or AI-assisted multimodal techniques for women with very dense breasts or high risk [1], [18]. Routine screening should begin at age 40 to 50 and continue until age 70, as advised by major guidelines, in accordance with evidence-based age

standards. To balance benefits, risks, and utilization of resources, screening decisions should be personalized within national health strategies for those over 70 [9], [18].

V. CONCLUSION

The problem of thick breast tissue often interferes with early cancer diagnosis using traditional mammography. To overcome this, sophisticated techniques, such as MRI, CESM, and DBT, are applied in order to increase the detection rates significantly. In areas where MRI is not available, additional modalities such as ultrasonography, CESM, and AI-assisted readings enhance the diagnostic accuracy. The next stage of screening is the combination of these state-of-the-art, multimodal technologies, particularly the CESM and AB-MRI, with individualized and risk-specific screening based on both genetic and clinical. This movement towards individualized care is beneficial to more equitable and cost-effective care, and ultimately results in improved clinical outcomes, reduction of mortality due to breast cancer, and is consistent with the significance emphasized by the recent 2024 USPSTF guidelines.

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