Minimally Invasive Breast Cancer: How to Find Early Breast Cancers

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Abstract

Purpose of Review Breast cancer, affecting over 2 million women annually, stands as the most prevalent non-skin cancer worldwide and ranks as the second leading cause of death in women. The 5-year relative survival rate decreases to 86% for regional breast cancer and drops significantly to 30% for distant breast cancer. Therefore it is critical to detect breast cancer early at the localized stage to minimize the morbidity and mortality associated with the diagnosis.

Recent Findings Considerable variability exists among radiologists in interpreting breast imaging, emphasizing the need for standardized guidelines to enhance reading accuracy and improve cancer detection rates. Factors influencing this variability encompass radiologists' familiarity with subtle findings of early and minimal breast cancer on screening modalities. Additionally, technologist factors, radiologist education, environmental considerations, workflow optimization, and the integration of artificial intelligence all contribute to impacting cancer detection rates.

Summary The interpretation of screening mammography and other imaging modalities is a complex process influenced by multiple factors. Radiologists must be cognizant of the diverse elements that can impact cancer detection for improved patient outcomes.

Keywords Minimally invasive cancer · Early detection · Annual screening · Educational requirements

Introduction

Breast cancer is the most common non-skin cancer in women worldwide, affecting over 2 million women annually, and the second leading cause of death in women [1]. According to the American Cancer Society (ACS), breast cancer accounts for about 30% of all new cancer diagnoses in women each year [2]. The ACS projections for 2023 in the USA indicate approximately 300,000 new cases of invasive breast cancer, along with an estimated 56,000 new cases of ductal carcinoma in situ [2].

Fifteen percent of the women diagnosed with breast cancer have a family history [3]. Those with a first-degree relative (mother, sister, daughter) with breast cancer are nearly twice as likely to develop breast cancer themselves [4]. The 5-year relative survival rate drops to 86% for regional breast cancer (cancer that has spread outside the breast to nearby structures or lymph nodes) and 30% for distant breast cancer (cancer that is spread to other parts of the body such as lungs, liver or bones) [5]. It is important to detect breast cancer early at the localized stage to minimize the morbidity and mortality associated with the diagnosis. Early detection of potentially fatal breast cancer enables earlier and more effective treatment.

This review explores several factors influencing early and minimal breast cancer detection and the enhancement of patient care. We define minimal breast cancer as localized cancer less than 1 cm in size. We will explore different radiologic modalities (including mammography, ultrasound and contrast-enhanced mammography, and MRI) for the detection of breast cancer, mammography being paramount. We delve into the importance of adhering to MQSA guidelines for the education and training of interpreting radiologists and technologists. The significance of a robust EQUIP (Enhancing Quality Using the Inspection Program) process is highlighted. Additionally, we examine other diverse elements such as patient factors, lesion characteristics, environmental influences, and radiologist biases, offering insights into understanding and mitigating potential errors. It is crucial to also acknowledge and address racial and ethnic disparities, actively working towards their correction.

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Mammography

Mammography remains the single most effective screening test for reducing breast cancer mortality, supported by numerous randomized clinical trials and large observational studies [6, 7]. These studies consistently demonstrate that mammography contributes to the reduction of breast cancer-related deaths [6, 7]. In the USA, the American College of Radiology (ACR) has implemented the Breast Imaging Reporting and Data System (BI-RADS) and the Mammography Quality Standards Act (MQSA) to maintain and enhance the quality of mammography.

The aim of screening mammography is to detect breast cancer at a localized stage with approximately 64% of breast cancer cases detected at this stage [5, 8]. The 5-year survival rate for cancer diagnosed at the localized age is 99% [5, 8].

By 2040, the burden of breast cancer is predicted to increase to over 3 million new cases each year and 1 million deaths every year [9]. This steady rise in breast cancer incidence is likely due to the aging population, but also more vigilant screenings and early detection efforts. Encouragingly, women who participate in screening mammography have demonstrated a statistically significant decrease in morbidity and mortality, suggesting that earlier detection through regular screening, along with advancements in treatment, have played a pivotal role in improving survival outcomes [10].

The inherent limitations in mammography that reduce both sensitivity and specificity lead to a miss rate of approximately 10–15% [11]. Medical errors are a substantial cause of morbidity and mortality and the third leading cause of death in the USA [12••]. In addition, missed breast cancer is one of the most common reasons for medical malpractice lawsuits against all physicians [12••, 13]. Investigators and prior studies have found up to 35% of both interval cancers and screen-detected cancers could be classified as missed [12••]. Herein, we discuss different factors involved in maintaining high accuracy and detection of early breast cancer and how to optimize those factors so as to enable a radiologist to achieve a higher cancer detection rate with a reasonable recall rate.

Screening Frequency and Patient Factors

The American Cancer Society, the Society of Breast Imaging, and the American College of Radiology recommend annual screening mammography beginning at the age of 40 for average-risk women and early initiation of screening mammography for high-risk women [14, 15]. In addition, screening mammography should continue past the age of 74 without an upper age limit unless significant comorbidities limit life expectancy [14, 15]. Maintaining annual screening

is critical with biennial screening missing the diagnosis of breast cancer in preclinical stages in nearly 2 of 3 women [16].

Various factors contribute to women not adhering to annual breast cancer screening recommendations, encompassing issues such as lack of health insurance, language barriers, misinformation regarding radiation exposure, limited access to mammography centers, and discomfort associated with mammograms [17, 18•]. Intriguingly, these factors often intertwine, as uninsured or underinsured individuals tend to experience poorer cancer outcomes than their insured counterparts. Disparities are evident, with African American and Hispanic women more likely to be uninsured compared to Caucasian women. Geographic barriers also play a role, disproportionately affecting underrepresented women. Notably, proximity to a mammography facility influences screening adherence, with those who missed annual mammograms residing farther away. African American and Hispanic women, more frequently facing economic challenges, tend to live at a greater distance from mammography centers [17, 18•].

It is important to understand that access to care is not universal and important to understand and implement strategies to counteract these problems. Mobile mammography along with other various for community outreach have shown to be beneficial. It is clear that the medical community and public health professionals must work together to promote health equality and improve access, education, and awareness of the annual screening.

Another factor that bears mentioning is the importance of creating an efficient and calm atmosphere for the patient. If the mammogram experience is quick, comfortable, and relatively non-traumatic, the patient is more likely to follow annual screening guidelines.

Lesion Factors

In a retrospective analysis of 172 prior mammograms, 80% of breast cancer demonstrated subtle nonspecific findings [19]. Breast radiologists must possess a keen awareness of nuanced indicators of early breast cancer, such as architectural distortion (with caution in interpreting negative ultrasound findings), and focal and developing asymmetry, particularly those apparent in the craniocaudal view, as seen in Fig. 1. A comprehensive approach involves scrutinizing evolving asymmetries by comparing current findings with mammograms from the past 5–7 years. Attentiveness to slowly growing subtle calcifications, especially in high-risk patients, is vital, necessitating a judicious recall threshold. It is imperative to verify the presence of all features characteristic of probably benign lesions before classifying a lesion as BI-RADS 3. Additionally, a nuanced understanding of

Fig. 1 Subtle breast cancer cases. **A** Imaging of a subcentimeter developing asymmetry best seen when comparing mammography from 2021 to 2022. **B** Imaging of a subcentimeter architectural distortion. **C** Imaging of a subcentimeter focal asymmetry
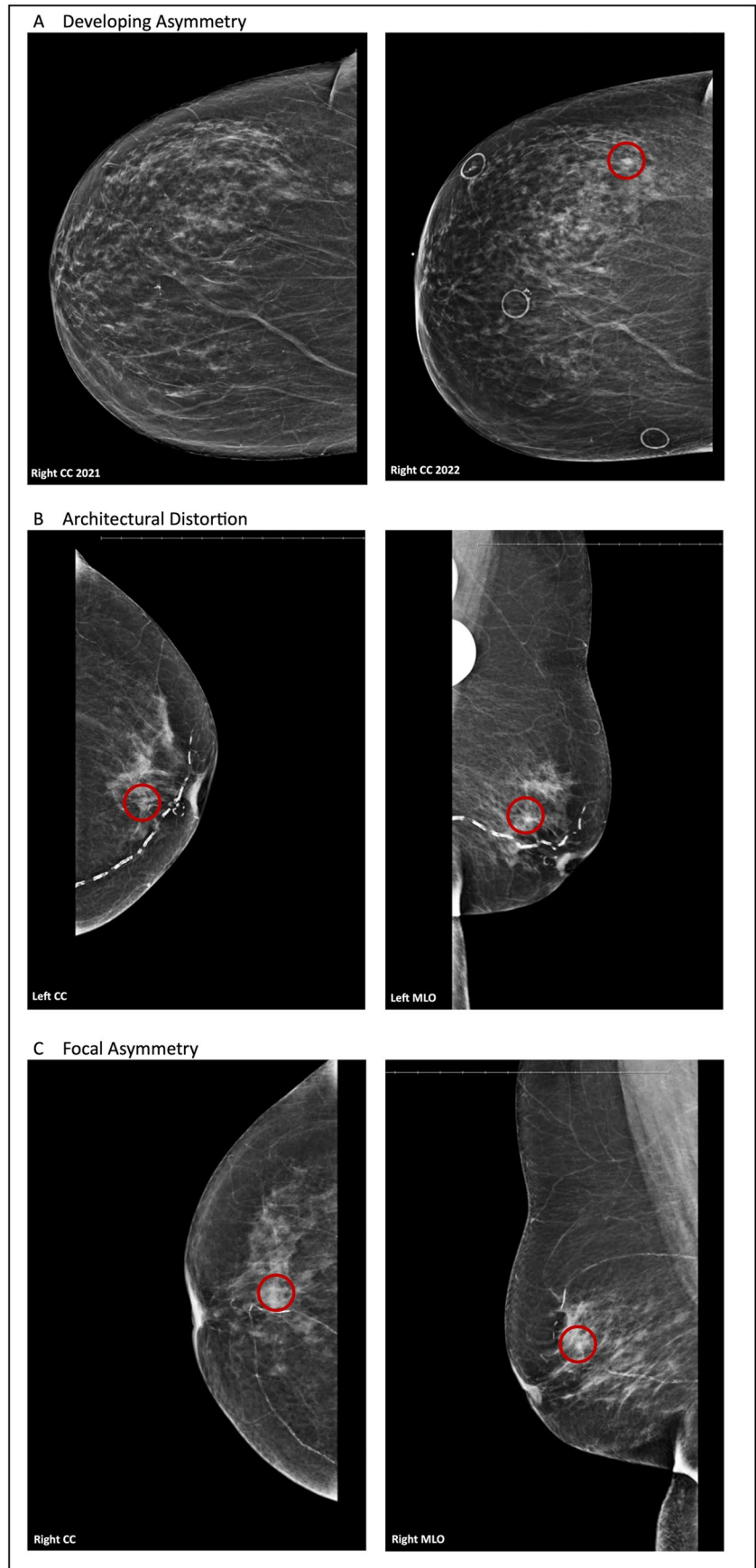
calcifications exhibiting indeterminate features, small groups of amorphous or coarsely heterogeneous calcifications, and the stability of lesions over at least 5–7 years is crucial for accurate interpretation.

It is important for the radiologist to be aware of cancers that typically manifest as circumscribed masses including medullary, mucinous, and papillary carcinomas, and metastases [12••, 20]. Invasive ductal carcinoma is not typically circumscribed but due to its frequency, it accounts for the majority of circumscribed cancers [12••, 20].

Radiologist Bias Factors

Radiologist bias factors play a pivotal role in the interpretation of mammograms, and a significant contributor to missed breast cancers is the lack of perception [12••]. To mitigate these biases, radiologists should adopt a systematic approach, practicing satisfaction of search by performing a secondary search after completing the primary search. Vigilance against inattention blindness, understanding blind spots and forbidden zones, and avoiding anchoring are crucial aspects of reducing errors. Radiologists should be encouraged not to hesitate to seek a second opinion and to resist premature closure, maintaining an open mind when formulating a diagnosis. Obtaining histopathology confirmation for findings that deviate from the criteria for benign or probably benign lesions is essential. Furthermore, avoiding satisfaction of reporting bias involves reviewing the examination without generating an impression before reading the prior report [12••, 21, 22].

Radiologist Educational Requirements

Fellowship-trained breast radiologists consistently exhibit a higher level of accuracy and CDR [23]. However, a significant portion of breast imaging interpretations in the USA are performed by general radiologists without specialized training in breast imaging [24]. While the MQSA mandates that radiologists interpreting breast imaging must have completed 12 full-time weeks of clinical breast imaging during their residency and interpreted 240 mammograms within any 6-month period within the last 2 years of residency, this standard may not suffice to bridge the gap in accuracy between fellowship-trained breast radiologists and general radiologists reading mammography.

Despite being from 1992, Linver and colleagues' audit revealed that attending an extensive 3- to 4-day instructor-led educational program in breast imaging led to a 50% increase in diagnosed breast cancers and a significant improvement in sensitivity, with no change in positive predictive value (PPV) [25]. A more recent randomized controlled trial by Geller and colleagues supports the idea that interpretive performance can be enhanced through educational interventions based on actual clinical cases with frequently misinterpreted findings [26]. These studies highlight the ongoing importance of education in breast imaging for both breast and general radiologists, emphasizing the need for continuing medical education courses. The notable disparities in accuracy between these two groups further advocate for additional training requirements to ensure consistently high-quality breast cancer screening.

Environment and Workflow

Correcting errors in mammography extends beyond technological solutions. False positives and negatives can also result from the reading environment. It is crucial to utilize physicist-approved radiologist workspace areas equipped with adjustable desks, ergonomic chairs, proper displays, and adequate lighting. Optimizing reading room conditions, such as controlling ambient lighting to reduce eye fatigue, is important. According to ACR recommendations, setting illuminance between 25 to 75 lx helps minimize specular and diffuse reflections on the workstation display [27, 28].

Adhering to the MQSA recommended guidelines and ACR Practice Parameters and Technical Standards for reading workstations is important in standardizing reading environments and improving detection rates. Similar adherence should be applied to mammography machines to ensure image quality. Rigorous compliance with these guidelines and undergoing annual MQSA inspections guarantee optimal working conditions and image acquisition for early detection.

Furthermore, an efficient workflow is critical during screening mammography readings. Workflow factors that can reduce errors in interpretation and improve accuracy include keeping track of prior cancer cases and performing a rigorous radiologic-pathologic correlation. Minimizing interruptions, uninterrupted batch reading, and double reading have consistently demonstrated improved breast cancer detection rates [29, 30]. A study even showed a 5–15% increase in cancer detection with double reading [30]. Although resources for double-reading all studies may be limited, establishing guidelines for double-reading images is a viable approach. Importantly, this is an area where AI can also provide valuable assistance.

Technologist Factors

Adequate training and maintenance of continuing education credits as per requirements of the MQSA should be adhered to. Continuous and random EQUIP process helps to maintain high-quality mammography images. It is also helpful to hire dedicated quality coaches who can improve positioning and technique for mammography technologists [31].

Indicators of proper positioning should be routinely used by the technologist to ensure adequate breast tissue coverage and image quality. For example, the mediolateral oblique (MLO) view should include the pectoralis muscle up to the nipple level, a convex contour of the pectoralis major muscle, complete visibility of posterior breast tissue, well-compressed breast tissue oriented in an up-and-out manner, and an open inframammary fold [32, 33].

In the craniocaudal (CC) view, the technologist must ensure the breast is drawn forward without excessive lateral exaggeration and adequately compressed. The variation in the measurement of the posterior nipple line between the mediolateral oblique and craniocaudal views should be limited to 1 cm. Prioritizing the upper outer quadrant, where most breast cancers are found, is essential. The technologist should employ the CC view alongside the mediolateral oblique view to also examine the medial tissue [32, 33].

Equipment

Digital breast tomosynthesis (DBT) has become the standard of care for screening mammography since its approval in 2011 by the Food and Drug Administration (FDA). DBT enhances cancer detection rates (CDR) while simultaneously reducing recall rates [34]. The 3D reconstruction capability inherent to DBT equips radiologists to more accurately characterize lesions that might otherwise trigger recalls in digital mammography interpretations. The amount of radiation to the breast can also be reduced by the use of two-dimensional synthetic images generated from the tomosynthesis deck. Synthetic two-dimensional images demonstrate comparable accuracy to conventional two-dimensional mammography imaging [35].

Artificial Intelligence

Considerable intra-reader variability exists in breast radiology, and the incorporation of artificial intelligence (AI) can effectively address this challenge [36]. Currently, AI, particularly computer-aided detection (CAD), is widely utilized in both screening and diagnostic mammography. The recent integration of sophisticated multilayered neural networks and machine learning has not only alleviated the workload of interpreting radiologists but has also significantly enhanced diagnostic accuracy [36, 37]. Although further prospective research is needed, AI-supported mammography screening has demonstrated a comparable cancer detection rate to standard double reading, accompanied by a substantially reduced screen-reading workload [38]. This suggests the safe and efficient use of AI in mammography screening.

Moreover, AI implementation facilitates the triage of screening mammography by identifying suspicious mammograms, ensuring prompt patient callbacks, and assisting in breast density assessments and breast cancer risk evaluations [39]. Additionally, AI contributes to maintaining image quality by offering real-time feedback to technologists [40].

The adoption of AI in breast radiology offers multiple advantages to radiologists, such as increased productivity, decreased burnout, and ultimately, improvements in cancer detection rates and patient outcomes [36–39].

The focus of AI development in breast imaging has predominantly centered on screening mammography; however, more recent investigations have expanded to include other breast imaging modalities such as ultrasound or MRI. For instance, a recent retrospective reader study assessing the performance of hybrid AI alongside radiologists in interpreting breast ultrasounds demonstrated preserved sensitivity for breast cancer detection. The hybrid AI workflow exhibited a significant advantage, reducing false positives by 37.3% and decreasing benign biopsies by 27.8% in the context of screening ultrasounds [41]. Additionally, another recent study reported non-inferiority between breast radiologists and an AI system in identifying malignancy in breast MRI [42]. Machine learning algorithms and AI are poised to play an increasingly significant role in various screening modalities, and radiologists should be well-prepared for this evolution [43].

Other Imaging Modalities

In addition to mammography, radiologists have access to various other breast screening tools. Table 1 presents sensitivity and specificity data from several studies on commonly employed imaging modalities. Table 2 provides statistics from different studies focusing specifically on patients with dense breasts, a context in which mammography exhibits lower sensitivity.

Breast Ultrasound

Breast ultrasound is a screening tool routinely utilized especially for dense breasts. It has been shown that per 1000 negative mammography screens, breast ultrasound will detect 2 to 5 additional breast cancers [44]. Breast ultrasound is performed using handheld ultrasound (HHUS) or with automated breast ultrasound (ABUS). ABUS was approved in 2012 by the FDA as a supplementary screening tool for women with dense breast tissue. The main advantages of ABUS are the increased standardization, decreased operator variability, and increased reproducibility of ultrasound imaging. Some studies have obtained a significantly higher detection rate in ABUS compared to HHUS [45].

Unfortunately, ABUS has limitations and disadvantages due to poor technique and artifacts [46]. The familiarity of the technician with proper positioning and compression

Table 1 Overall sensitivity and specificity of different imaging modalities [47–50]

Study	Participants (N)	Imaging	Sensitivity (%)	Specificity (%)
Gonzalez-Huebra et al. (2019)	N=280	MG	52.5	–
		MG+US	82.5	–
		MG+DBT	72.5	–
		MG+US+DBT	96.4	–
		MRI	94.3	–
Chen et al. (2021)	N=475	MG	72.4	–
		US	88.6	–
		MG+US	93.1	–
Kim et al. (2022)	N=1452	Abbreviated MRI	100	93
		Full-Protocol MRI	69	86
Lawson et al. (2023)	N=246	CEM	61.1	87.8
		Abbreviated MRI	88.9	75.7
		Full-Protocol MRI	100	80.2

Abbreviations: *MG* digital mammography, *US* ultrasound, *MRI* magnetic resonance imaging, *DBT* digital breast tomosynthesis (3D mammography), *CEM* contrast-enhanced mammography

Table 2 Performance of different imaging modalities on high breast density patients [51–54]

Study	High breast density participants (N)	Imaging	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Berg et al. (2012)	N=2725	MG	46.3	90.8	–	–
		US	56	84.9	–	–
		MRI	87.5	75.7	–	–
		MG+US	71.4	80.9	–	–
		MG+MRI	100	70.6	–	–
		MG+US+MRI	100	65.4	–	–
Shao et al. (2013)	N=49	MG	72.7	62.9	75.5	59.5
		US	80	62.9	72.9	65.6
		MRI	90.9	82.7	89.3	85.3
		MG+MRI	92.3	51.4	65.4	85.7
		US+MRI	94.5	65.7	78.3	88.5
		MG+US+MRI	98.2	37.1	51.1	92.9
Chou et al. (2015)	N=53	US	61	87	81	71
		MRI	96	77	79	96
Gonzalez-Huebra et al. (2019)	N=155	MG	42.7	–	–	–
		MRI	92.3	–	–	–
		MG+US	79.6	–	–	–
Phalak et al. (2019)	N=72	MG	33	77	17	89
		US	55	95	60	94
		MG+US	83	72	29	97

Abbreviations: *MG* digital mammography, *US* ultrasound, *MRI* magnetic resonance imaging, *PPV* positive predictive value, *NPV* negative predictive value

by changing the receptor plate based on breast size and the interpreting breast radiologist with these artifacts will decrease false negative diagnoses of true lesions.

As seen in Tables 1 and 2, the sensitivity and specificity of ultrasound are higher than that of mammography in multiple studies [47–54]. When ultrasound is added to mammography or mammography and MRI, the sensitivity and specificity increase further [47–54]. Thus the use of ultrasound should be considered in all patients, not just in cases with dense breast tissue.

Magnetic Resonance Imaging (MRI)

Contrast enhancement is based on the principle of tumor new angiogenesis wherein breast cancer typically demonstrates rapid washing and washout. The contrast enhancement is useful for resolving equivocal findings on conventional imaging and as a screening method for high-risk patients.

As seen in Tables 1 and 2, the average sensitivity of breast MRI is higher than the sensitivity of mammography and ultrasonography based on multiple different studies, with MRI yielding additional cancers not otherwise detected by mammography and/or sonography [47–54]. The long scan time, need for IV contrast, and limited access to MRI scanners currently limit breast MRI as a feasible screening modality other than for high-risk patients. Abbreviated MRI protocols have emerged in recent years wherein the duration of the breast MRI is decreased and have shown to have comparable accuracy to conventional breast MRI. In fact, a recent study showed screening of high-risk women with abbreviated breast MRI showed comparable sensitivity and superior specificity to the full-protocol MRI [49].

Contrast-Enhanced Mammography

More recently, contrast-enhanced mammography has emerged as a technique that uses iodinated contrast materials for the visualization of breast neovascularity in a fashion similar to MRI [55]. Preliminary studies have shown that contrast-enhanced mammography had lower recall and higher specificity compared with standard MRI or abbreviated MRI, offset by lower cancer detection rate and sensitivity compared with standard MRI, as seen in Table 1 [50]. Benefits of contrast-enhanced mammography over abbreviated MRI include cheaper cost as an MRI machine is not necessary, with similar exam time lengths.

While additional prospective studies are required to determine the optimal use of these new imaging modalities, radiologists should be aware of them and consider their application, particularly in high-risk patients.

Conclusion

Breast cancer is the most common cancer in women worldwide and the second leading cause of cancer death in women. Early detection of localized minimal breast cancer has a significant impact on patient morbidity and mortality. In the above review, we have discussed various ways and means to aid in the early detection of breast cancer with annual screening mammography initiated at the age of 40 and average-risk women being one of the most important factors.

Furthermore, techniques to detect breast cancer early using subtle signs of early breast cancer as well as the optimization of patient factors and environmental factors have been discussed.

Supplemental screening tools like ultrasound and contrast-enhanced mammography as well as contrast-enhanced MRI have also shown promise to help decrease missed minimal breast cancer. Our ultimate goal is to help mammography programs understand the limitations and ways and means to optimize early detection by using a multidimensional approach.

The interpretation of screening mammography is a multifaceted process influenced by many factors. It starts with the quality and precision of the mammography machine itself, followed by the expertise and competence of the radiology technician conducting the examination. Additionally, the workflow and environment within which the interpreting radiologist works play a crucial role in the accuracy of interpretation.

Declarations

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Papers of particular interest, published recently, have been highlighted as:
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•• Of major importance

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