



## Review Article

# Breast cancer screening programs: Review of merits, demerits, and recent recommendations practiced across the world



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## ABSTRACT

Breast cancer screening is defined as the evaluation of symptom free, otherwise healthy looking females of child bearing age or postmenopausal women for early detection of breast cancer. Screening mammography is the most common and widely practiced breast cancer screening modality across the world. The other modes of breast cancer screening being practiced across the world are: breast self-examination (BSE), clinical breast examination (CBE), digital breast tomosynthesis (DBT), ultrasonography (USG), magnetic resonance imaging (MRI), and identification of certain genetic oncogenes. The major merits of breast cancer screening programs are: early diagnosis, sorting out and prevention of risk factors, and timely treatment to lessen the morbidity (5 years localized stage survival rate is 99%, regional disease 84% while metastatic breast cancer 5 year survival rate is 23%); it also reduces overall 20% mortality rate. The major demerits of breast cancer screening are: overdiagnosis (19% from the perspective of a woman invited to screening), high cost, ionizing radiation (lifetime attributable risk to develop breast cancer is 3/10,000), false positive biopsy recommendation (about 8/1000), false negative results 11/10,000, and their consequences. Worldwide, most of the countries recommend biennial screening for breast cancer at 50–74 years of age. However, some countries recommend screening mammography earlier, starting at the age of 40 years until 70–74 years based on higher breast cancer incidence rate in those countries. This article provides a detailed review of merits, demerits, and recent recommendations for screening programs being practiced across the world.

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## 1. Currently used breast cancer screening tools

According to the most recent data available, breast cancer is the most common cancer among women worldwide [1–3].

In 2012, across the world 1.7 million new cases were diagnosed. In 2014, local cancer registry data indicates that

breast cancer incidence is probably higher in the Kingdom of Saudi Arabia (KSA) than those countries in which most of the studies are conducted [4].

Breast cancer was estimated to be detected among 232,000 women in the United States in 2015 and 40,000 women died of it [5]. Breast cancer is the most frequently diagnosed cancer among women aged 55–64 years with the median age of death at 68 years. This alarming breast cancer death rate of 6.8% as opposed to all cancers death rate necessitates the endorsement of breast cancer screening programs for early detection and prompt treatment for breast cancer.

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Screening mammography is the most common and widely practiced breast cancer screening tool worldwide [6,7].

The other different modes of breast cancer screening being practiced across the world are: breast self-examination (BSE), clinical breast examination (CBE), digital breast tomosynthesis (DBT), ultrasonography (USG), magnetic resonance imaging (MRI), and identification of certain genetic oncogenes mutations.

BSE is done by the female herself to find lumps or other abnormal feelings in the breast, while CBE is done by a doctor or healthcare provider. The potential benefits of both of these are not convincing to reduce the mortality rate and there is no consensus by experts to recommend them widely in breast screening [8].

Mammography is visualization of breast tissue by the use of low dose X-rays either as a screening mammography or as diagnostic mammography. It is recommended mostly in elderly women, usually at the ages of 50 years and 75 years [9]. Mammography usually is not a routine screening modality in females younger than 40 years, in part due to the dense glandular tissue as well the hazard of ionizing radiation. Although cost-effective, it is the most widely practiced screening tool for breast cancer among women older than 40 years.

DBT is like digital mammography. In DBT, dozens of thin cross-sectional images are combined with conventional X-rays, and three-dimensional (3-D) images are developed. This technique is more beneficial for women with dense glandular tissue. The Food and Drug Administration (FDA) approved DBT in 2011 for screening breast cancer [10].

USG is another screening modality most often recommended in younger women with dense glandular tissue, especially those with mammographic microcalcifications and clinically suspicious breast lumps.

MRI is not a widely practiced breast cancer screening modality, as it is not cost-effective and there is a lack of facilities for large population-based screening programs. Moreover, there is no promising evidence to support its role as a breast cancer screening tool across the world.

BRCA oncogene detection revealed that there are greater chances of breast cancer to develop among those patients who have previously had breast cancer, a family history of breast cancer, and ovarian cancer. However, BRCA oncogene detection does not confer breast cancer in patients with positive mutations or who have a family history of breast cancer.

Overdiagnosis [11] and overtreatment of breast cancer among normal women and its psychosocial impact on their personalities limited widespread use of breast cancer screening programs and favors recent restrictions for breast cancer screening practiced across the world. A detailed discussion of merits and demerits of breast cancer screening programs, recommendations, recent restrictions across the world, and consequences of overdiagnosis are reviewed in this article.

Other objectives of this article are to determine the role of different breast cancer screening programs practiced across the world for diagnosis of breast cancer in different age groups, and to review different recommendations for breast cancer screening, the merits and demerits, and

impact of overdiagnosis of breast cancer among healthy women who underwent a screening process.

## 2. Discussion

For the purpose of discussion, risk stratification for development of breast cancer among women is as follows [12]. High risk women are those who have four times greater risk than the normal population and these are: bilateral premenopausal breast cancer, family history of breast cancer in mother, sister, child, or close relative, genetic mutation of BRCA 1 and BRCA 2 genes, lobular carcinoma *in situ*, atypical hyperplasia, and > 75% mammographic density of breast volume.

Average risk women are those who have two to four times greater risk than the normal population and these are: Northern European and North American residents, older age, personal history of breast cancer, premenopausal breast cancer in family, hyperplasia without atypia, and > 50% mammographic density of breast volume [12].

Low risk women are those who have less than two times risk of normal and these are: nulliparity, age of menarche < 11 years, first birth after 30 years, age of menopause > 55 years, family history of postmenopausal breast cancer, high socioeconomic status, postmenopausal obesity, and daily alcohol consumption [12].

Aberrations of normal development and involution are a series of developmental changes and involution process taking place in the female breast during different ages. These developmental changes during different ages highly influence the screening process and have variable positive predictive values among different age groups (Figures 1–4) [13] (mammographic) represent variable proportions of different breast tissues in different age groups.

More than 75% of the lymphatic drainage of the breast is through axillary lymph nodes, although a significant proportion drains through intercostal lymphatics to the opposite breast and subdiaphragmatic lymphatics to the liver. Moreover, breast cancers metastasize mainly to the draining lymph nodes, but osseous metastasis primarily involves the thoracolumbar spine, brain, lungs and liver.

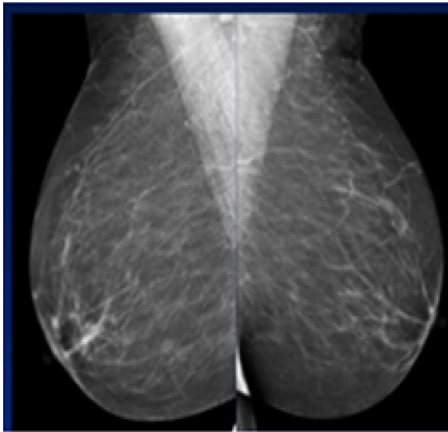
The following breast cancer screening modalities are discussed in detail: (1) BSE; (2) CBE; (3) mammography; (4) DBT; (5) USG; (6) MRI; (7) BRCA oncogenes.

### 2.1. BSE

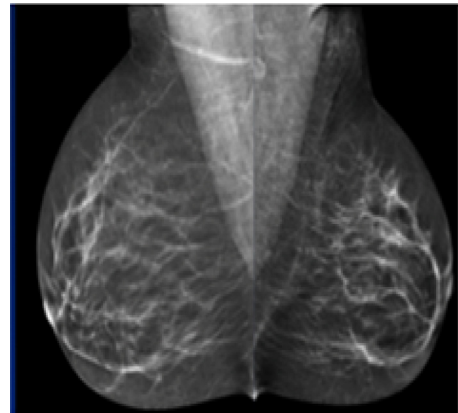
BSE is the physical examination of the breast by females themselves. It is a noninvasive and inexpensive technique. Women are taught how to perform BSE. It is recommended every month, 1 week after the start of the menstrual period usually from the 6<sup>th</sup> day to the 10<sup>th</sup> day of the menstrual cycle, when breast swelling and fibrocystic changes are less likely to interfere with the detection of a lump or mass.

#### 2.1.1. Merits of BSE

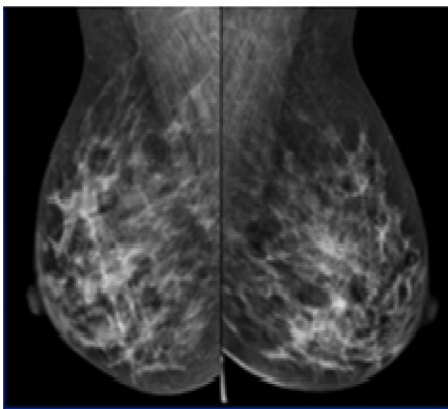
BSE examination benefits females as they can inform their clinician or healthcare provider of any change in color of skin, nipple discharge, recent nipple inversion, skin dimpling, any lump, swelling of a part of the breast, and any abnormal feeling in axillae, in a timely manner. The other



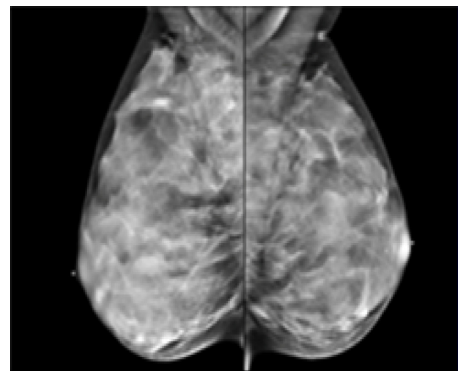
**Fig. 1.** Almost entirely fat <25% glandular [9].



**Fig. 2.** Scattered fibroglandular 25–50% glandular [9].



**Fig. 3.** Heterogeneously dense 50–75% glandular.



**Fig. 4.** Extremely dense >75% glandular.

merits of BSE are that it enables women to be well aware of breast problems and it helps women to assess the consistency of their own breasts and to learn the skills of breast examination.

#### 2.1.2. Demerits of BSE

Once, BSE was promoted to discover breast cancers in women, but in several controlled studies it has been declared that the efficacy of BSE as a breast cancer screening tool is not convincing and BSE could not help to reduce breast cancer mortality [10]. Furthermore, it is stated that it may result in depression, anxiety, additional imaging procedures, and biopsies with scarring that may prevent early detection of future breast malignancy.

#### 2.1.3. Recommendations

A meta-analysis study published by the *Cochrane Collaboration* in 2008 done in China and Russia on 380,000 women did not show advantages in women who performed BSE regularly when compared with those who did not [14].

In 2014, based on a lack of evidence and high level of uncertainty, The Ministry of Health of Saudi Arabia guideline panel recommended that BSE could not be applied as a single breast cancer screening method among women of all age groups [15].

Several international organizations like the World Health Organization, United States Preventive Services Task Force (USPSTF), American Cancer Society (ACS) [16], American Academy of Family Physicians, and Canadian Task Force on Preventive Health Care, did not recommend teaching women how to do BSE, because the evidence concludes that training females for BSE does not reduce the breast cancer mortality rate. The USPSTF supports that all women should be aware of changes in their bodies and should be encouraged to discuss these changes with their clinicians, however, in February 2016, the USPSTF did not update its 2009 recommendation on teaching BSE [17].

The American College of Obstetricians and Gynecologists (ACOG) [18] and American Medical Association, however, recommend monthly BSE and suggest that females should be familiar about their normal breast feeling, so that they can detect any abnormality to point out earlier to health care providers or clinicians.

#### 2.2. CBE

A comprehensive CBE includes detailed history, physical examination by inspection, palpation of breast in different positions, and lymph nodes examination by the clinician or healthcare provider.

### 2.2.1. Merits of CBE

The benefits or merits of CBE are that it helps to evaluate masses and skin changes in the breast noticed by the females, to detect masses that are missed during routine screening mammography, and to discover lesions that may appear in between the next screening appointment. It also helps to differentiate between benign and malignant breast lesions, assess the stage of disease, counsel the patient, plan effective treatment, and document the clinical data for audit and follow up.

### 2.2.2. Demerits of CBE

Worldwide, no clinical trials have been done to evaluate the efficacy and sensitivity of CBE alone. Evidence from various clinical trials indicates that CBE combined with mammography helps to increase screening sensitivity, especially among younger women with more glandular tissue, as mammography is less effective among women who underwent mammography twice yearly as compared to annually [19].

### 2.2.3. Recommendations

In 2014, based on a lack of evidence and high level of uncertainty, The Ministry of Health of Saudi Arabia guideline panel recommended that CBE by a health care professional could not be applied as a single method of breast cancer screening among women of all age groups. The panel recommended that screening mammography is the first choice for breast cancer screening if available, however, CBE could be offered only when screening mammography is not available [15].

The ACOG recommended that CBE should be done three times yearly for women aged 20–39 years and annually for women aged 40 years or older [18].

A recent study performed in a rural community in Malaysia declared that CBE detects > 50% of the breast cancers seen on screening mammography and may help to improve survival rates from breast cancer, especially in those areas where mammography is not available [20].

In 2009, the USPSTF recommended that there are no extra advantages or disadvantages of CBE, except screening mammography, among women aged  $\geq 40$  years. In February 2016, the USPSTF did not update its year 2009

recommendation on the additional potential benefit of CBE [11,17]. ACS guidelines in 2015 did not recommend CBE for women at any age with average risk [16].

## 2.3. Mammography

Mammography is the most widely accepted breast cancer screening modality being practiced across the world. Mammography is the visualization of breast tissue by use of low dose X-rays either as a screening mammography or as the diagnostic mammography. The diagnostic mammography helps to diagnose the symptoms experienced by women attending the clinic or called back for follow up, while the screening mammography is recommended for detection of and sorting out breast cancers on population-based programs. At present, there are modifications in usual mammographic X-ray images taken on plain films. Recently, images have been taken on computer screens and this is called digital mammography. Digital mammography appeared to be better in dense breasts with lower doses of radiation than conventional mammography [21]. However, numerous studies have found little or no difference between conventional mammography and digital mammography, despite the higher cost of the digital system, and both are equally effective. Computer aided detection by the use of computer software may slightly increase sensitivity of digital mammography, but at the expense of reduced specificity and repeated visits [22].

Figures 5A and 5B visualize invasive breast cancer lesions demonstrating calcification with spicules radiating in all directions from abnormal mass [9].

Microcalcifications appear in areas of rapidly growing cells and are diagnostic for cancerous lesions, however, macrocalcifications are a normal finding among women aged 50 years and older. Among all ages, screening mammography has a sensitivity of approximately 77–95% and a specificity of 94–97% [23].

### 2.3.1. Merits of mammography

The merits of mammography are as follows. Early detection of breast cancer [24] and lower stage benefits in terms of decreased morbidity, as the cancer is treated by less

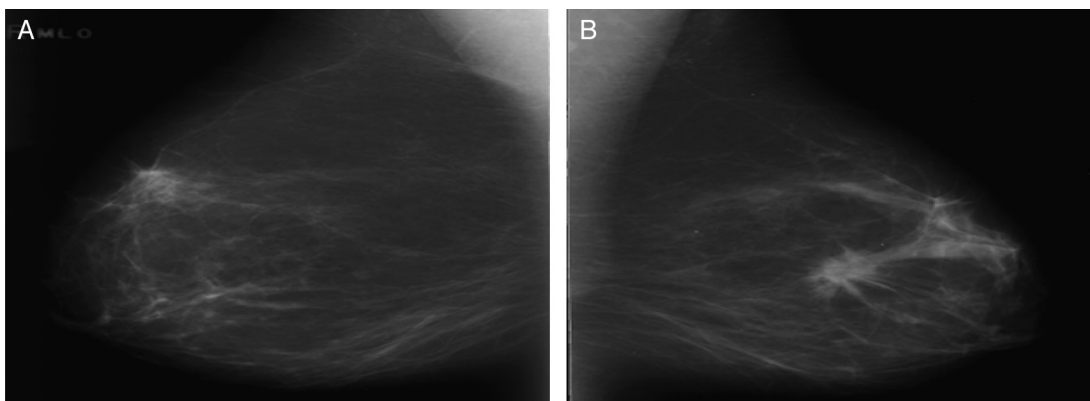
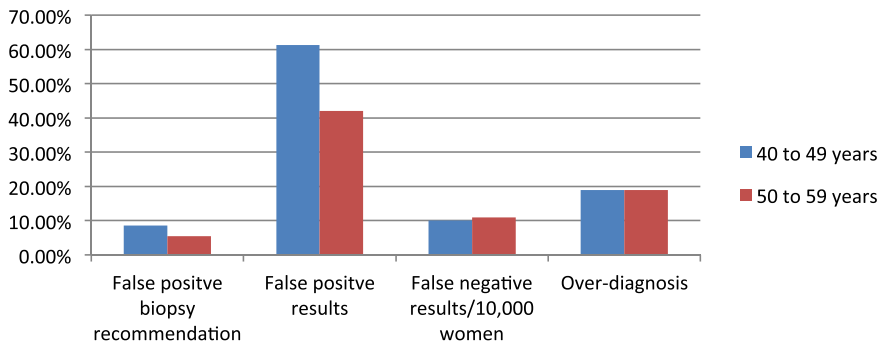


Fig. 5. (A,B) Mammography highlighting speculated mass in the left breast [9].



**Fig. 6.** Indicating false positive biopsy recommendation, false positive results, false negative and overdiagnosis.

toxic therapy with breast conservation surgery, more often without chemotherapy [25].

Better 5 year survival rates in early detection of breast cancer at a lower stage with endorsement of early treatment have been proven, with better survival rates; the 5 year localized stage survival rate is 99%, regional disease 84%, and metastatic breast cancer 5 year survival rate is 23% [26].

Reduced mortality rates were observed in a meta-analysis of 11 trials with 13 years of follow-up, with an estimated 20% reduction in mortality rate from breast cancer in women invited for screening [26], as well as substantial benefits in reducing the breast cancer death rate [17].

Decreased breast cancer death rates that can be avoided in different age groups by means of mammography as breast cancer screening modality are; 3% among women aged 40–49 years, 8% in women aged 50–59 years, 21% among women aged 60–69 years, and 13% in women aged 70–74 years [17].

### 2.3.2. Demerits of mammography

The demerits of screening mammography are as follows. The potential harm of early detection of precancerous lesions like ductal carcinoma *in situ*, which may result in multiple biopsies for confirmation or unnecessary treatments, although it may not progress to invasive breast cancer for the remaining life period.

False-positive biopsy recommendation after screening mammography in a cumulative study published in February 2016 by the USPSTF states that the biopsy rate with annual and biennial screening among females aged 40–49 years is 7–9.4%, while it is 4.8–6.4% among women aged 50–59 years [17].

Another demerit of screening mammography is detection of noninvasive cancer that will never lead to death or threaten the life of women in the absence of screening. This may not only cause psychological and behavioral changes, but also results in additional visits. Furthermore, false positive results may also cause anxiety and additional cost.

Results from a 10 year cumulative study issued by Breast Cancer Surveillance Consortium Registry Data published by the USPSTF concludes that false positive results are 61.3% among females aged 40–49 years and 42% among women aged 50–59 years [17].

The frequency of overdiagnosis was 11% from a population perspective, and 19% from the perspective of a woman invited to screening [26]. According to this study which lasted for 10 years, one in five women were overdiagnosed as having breast cancer; the final recommendation statement on breast cancer screening published in February 2016 by the USPSTF stated that, although it is not possible and even difficult to predict what percentage of women may develop cancer during later life, the abovementioned overdiagnosis rate should be accepted [17].

False negative results that may delay diagnosis; the disease process attains an advanced stage and the delayed treatment makes the undiagnosed patient prone to resultant increased morbidity as well as early death. Breast Cancer Surveillance Registry Data states that one time mammography/10,000 women results in false negative mammograms among women aged 40–49 years, 50–59 years, 60–69 years, and 70–74 years in 10%, 11%, 12.5%, and 15%, respectively [17]. Figure 6 graph is plotted from the above data [17].

The overall risk of ionizing radiation exposure, although small, depends upon how many times the patient experiences ionizing radiation exposure during a lifetime [22]. The lifetime attributable risk from radiation to develop breast cancer after 2 yearly screening mammography among women aged 50–74 years is three per 10,000 women screened [17].

There are certain limitations of mammography such as mammography is not usually recommended for a pregnant woman, and it cannot be performed in breastfeeding women because milk shadows may resemble fine microcalcified opacities. Breast implants or scar tissues may interfere with radiographic interpretation.

### 2.3.3. Recommendations

Worldwide recent recommendations for mammography by different organizations are as follows. In 2014, based on local cancer registry data that states that breast cancer incidence is probably higher in KSA [15] than those countries in which most of studies were conducted, the Ministry of Health of KSA guideline panel recommended screening mammography for breast cancer among women aged 40–49 years every 1–2 years. The same panel recommended biennial screening mammography for breast cancer screening at the age of 50–69 years, however, the

panel did not recommend mammography as a breast cancer screening program at the age of 70–74 years.

The USPSTF recommend that biennial screening mammography should be started at the age of 50 years, as the evidence is convincing that screening mammography started at this age results in reduced mortality rate. The absolute mortality reduction rate is greater among women aged 50–74 years compared with those aged 40–49 years, however, women aged 60–69 years have the greatest advantage of reduction in mortality rate. The USPSTF does not recommend screening mammography among women < 40 years old, however, women aged 40–49 years with high risk, such as first degree relatives like sibling, child, or parent, may benefit more than average risk women by screening mammography starting before the age of 50 years and the decision to advise screening mammography should be well informed, individualized after she weighs the potential benefits and harm. The USPSTF concludes that there are no benefits of screening mammography after 74 years of age [17].

The Canadian Taskforce on Preventive Health Care recommended screening mammography at the age of 50–74 years. They concluded that the decreased mortality rate associated with screening mammography is not significant at the age of 40–74 years who are at average risk of breast cancer, however, women aged > 50 years when compared to women aged < 50 years benefit more from screening mammography. Moreover, the potential harmful effects of overdiagnosis and extra biopsies are greater in younger women than elderly women [27].

The Nordic Cochrane Centre stated that trials of screening concluded that screening saved lives, but at the cost of considerable harm due to overdiagnosis [28]. The American Cancer Society recommended yearly screening mammography at 45 years of age, but it can be optionally started at the age of 40 years and the decision to start screening is individual among high risk women. At the age of 55 years, it is optional to continue as annually or biennial. This biennial screening mammography should be continued as long as the health of woman is well with life expectancy of 10 years or more [29]. The American College of Obstetricians and Gynecologists recommended that screening mammography should be started at the age of 40 years annually and after 75 years, women should consult their physicians about whether to continue or not [30].

The American Cancer Society [29] along with several other organizations, including the American Academy of Family Physicians [31], the Well-Woman Task Force assembled by the American Congress of Obstetricians and Gynecologists [32], the Canadian Task Force on Preventive Health Care [27], and the American College of Physicians [33] also recommended that initiating screening breast cancer at the age of 40 years is an individual decision.

In the United Kingdom, the National breast cancer screening programs, Finland, Denmark, Poland, Switzerland, The Netherlands, Norway, Germany, Belgium, and Luxembourg, recommend screening mammography for breast cancer after every 2–3 years for women aged 50–74 years [34]. Many European countries favor recommendations of the International Agency for Research on Cancer, which in 2015 updated its guidelines to promote

breast screening and which should be started at the age of 50 years [35].

The Cancer Council of Australia recommends mammography at the age of 50–74 years every 2 years, however, women aged 40–49 years and older than 74 years are allowed for screening, but not invited by invitation letters. Mammography is the recommended breast screening tool for the early detection of breast cancer [36].

South Africa does not have any official breast cancer screening program, although the Cancer Association of South Africa stated that the lifetime risk of breast cancer in African women is one per 33 [37].

In China, at present there is no nationwide breast cancer screening program, although it was started in 2005 when 100,000 women were screened by mammography and USG, but stopped due to false positive results and insufficient funding [38].

In Russia, mammography screening is recommended at 40 years of age biennially with two view mammography and for a single time [39].

The latest restrictions on screening mammography are by Gøtzsche PC and Jørgensen K [28], and they published a study; Screening for breast cancer with mammography Nordic Cochrane Center on 4 June, 2013 that recent observational studies from eight randomized control trials for 10 years declared that overdiagnosis and unnecessary treatment is 30% and mortality reduction rate is 15%. If we presume that screening mammography decreases the breast cancer mortality rate by 15%, but the overdiagnosis and overtreatment is 30%, this means that for every 2000 women who underwent screening for 10 years, one will be prolonged for breast cancer, but 10 women will be treated unnecessarily. Moreover, in this published literature they concluded that women should be well informed about the benefits and harm of screening mammography before they attend screening [28]. Summary of worldwide recommendations is given in tabulated form in Table 1.

Implementation of breast cancer screening programs in low- and middle-income countries is very complex. Lack of surveillance and monitoring systems are the major problems to formulate a policy regarding breast cancer screening in these countries [40]. At present, the best option ahead for low- and middle-income countries is to start an opportunistic screening mammography combined with CBE. However, use of USG as a breast cancer screening modality in these countries is eagerly awaited.

## 2.4. Tomosynthesis

DBT is like digital mammography. In DBT, dozens of thin cross-sectional images are combined with conventional X-rays, and three-dimensional images are developed.

### 2.4.1. Merits of DBT

The advantages of DBT are that images can be taken separately and examined individually which lessens the overlapping problem of images. These provide more sophisticated images, better locates the lesion, provides more accurate information about its shape and size, and decreases revisit frequency [41]. This technique is more

**Table 1**  
Summary of worldwide recommendations for breast cancer screening programs by different organizations.

Name	BSE	CBE	Mammography	USG/ DBT	MRI	BRCA genes
<b>MOH KSA [15]</b>	BSE could not be applied as a single breast cancer screening method among women of all age groups	CBE by a healthcare professional could not be applied as a single method of breast cancer screening	40–49 y every 1–2 y 50–69 years biennial No at 70–74 y	No Recommendation	No	Worldwide BSE every mo, CBE twice annually, annual mammography & MRI starting at the age of 25–30 y
<b>USPSTF [17]</b>	Did not update its 2009 recommendation on teaching BSE	Did not update its 2009 recommendation on teaching CBE	50–74 y annually High risk individual At 40–49 y	As supplemental With mammography in dense breast	As supplemental With mammography in dense breast	
<b>ACS [29]</b> <b>CTPHC [27]</b> <b>ACOG [30]</b>	Same as above Same as ACS Recommend monthly BSE	Same as above Same as ACS Recommend 3/y for women aged 20–39 y and annually for women aged ≥40 y	Same as above Same as above At 40–75 years, Annually. After that consult physician	Same as above Same as above	Same as above Same as above	
<b>UK [34]</b>	No recommendation BSE	No BSE	50–74 y biennial	Same as above	Same as above	
<b>CCA [36]</b>	Same as above	No BSE	50–74 y biennial	Same as above	Same as above	
<b>CHINA [38]</b>	No advantage of BSE	No advantage of CBE	No screening	Same as above	Same as above	
<b>RUSSIA [39]</b>	No advantage of BSE	No advantage of CBE	40 years biennial	Same as above	Same as above	

ACOG = American College of Obstetricians and Gynecologists; ACS = American Cancer Society; BSE = breast self-examination; CBE = clinical breast examination; CCA = Cancer Council of Australia; CTPHC = Canadian Taskforce on Preventative Health Care; DBT = digital breast tomosynthesis; MOH KSA = Ministry of Health Kingdom Of Saudi Arabia; MRI = magnetic resonance imaging; USG = ultrasonography; USPSTF = United States Preventive Services Task Force.

beneficial for women with dense glandular tissue. The FDA approved DBT in 2011 for screening breast cancer [42].

#### 2.4.2. Demerits of DBT

The major demerit of DBT is prolonged time and more radiation exposure (twice that of standard mammography) although it minimizes the urge for repeat mammographic images. Furthermore, it leads to more biopsies recommendation rates [43].

#### 2.4.3. Recommendations

There is only a single prospective cohort study for evidence of DBT as a primary breast cancer screening modality. The number of patients screened was 7292 from a screening population from two cities, based on comparison of digital mammography alone and combined with DBT. According to this study, digital mammography had a sensitivity of 0.54 [95% confidence interval (CI), 0.42–0.65] compared with 0.85 (95% CI, 0.74–0.92) for DBT, while the specificity for digital mammography was 0.96 (95% CI) and 0.97 (95% CI) for DBT with digital mammography. The cancer detection rate was 4.8/1000 women with digital mammography and 7.4/1000 women with DBT with digital mammography [39]. In the light of the above single study, in February 2016, the USPSTF published a recommendation summary and stated that there is insufficient data to weigh the merits and demerits of DBT as a primary breast cancer screening method and continuous research should

be done before DBT can be recommended as a breast cancer screening modality worldwide [44].

#### 2.5. USG

USG is high frequency sound waves in the form of images on a viewing screen. It is usually recommended for women with denser breasts. Ultrasound is used to evaluate breast abnormalities which are detected with screening mammography or during a physician performed breast examination. Figures 7–10 illustrate USG images [9] for a simple cyst, a complicated cyst, a solid lesion, and a complex lesion, respectively.

Recently, the FDA approved Automated breast US as a screening tool for breast cancer [45], yet, it is used as a first line modality in women younger than 30 years when a breast abnormality is found secondary to the large amount of fibrous tissue found in women of this age.

It is also recommended as a supplemental tool in those women that are screened by mammography and among women with dense breast who do not meet the criteria of MRI as a screening modality. The sensitivity of USG for women with negative screening mammography is 80–83% and specificity range 86–94%, with a positive predictive value of 3–8% [46].

##### 2.5.1. Merits of USG

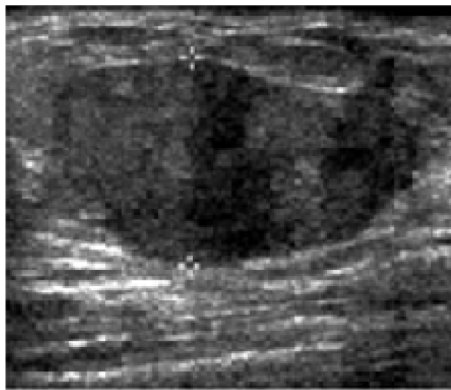
The major advantages of USG are as follows. It allows significant freedom in obtaining images of the breast from



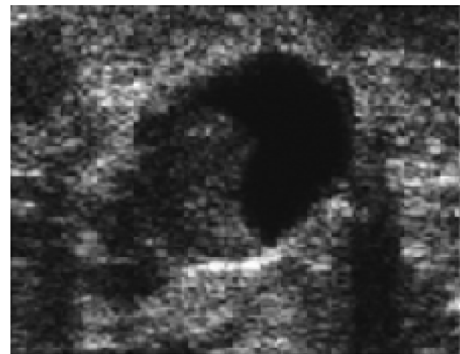
**Fig. 7.** Simple cyst.



**Fig. 8.** Complicated cyst.



**Fig. 9.** Solid lesion.



**Fig. 10.** Complex lesion.

almost any direction. It is noninvasive, with no radiation exposure, and can be practiced in younger women with dense breast, as well as during pregnancy. It is economical and patient friendly. It can be good in identifying cystic disease and can assist in therapeutic aspiration as well needle biopsy of solid tissue lesions and fine needle aspiration cytology.

#### 2.5.2. Demerits of USG

The major disadvantages of USG are as follows. It lacks spatial resolution and fine detail. It cannot detect most calcium deposits on breast tumors. It cannot document how much breast tissue has been imaged. USG usually will not identify lesions < 1 cm. It is a highly operator-dependent tool and necessitates the need of a skilled sonologist, high-quality examinations, and state of the art equipment.

#### 2.5.3. Recommendations

As stated above, USG is not approved as a single screening modality by the FDA and no international organization recommended USG as a primary breast cancer screening modality. However, it is an emerging tool for breast cancer screening. Presently, it is used as an adjunct with screening mammography for breast cancer screening in denser breasts, especially in younger women who have more glandular tissue. A study was conducted in China from 2008 to 2010 at 14 breast centers. A total of 13,339 high-risk women aged 30–65 years were

randomly screened by USG alone, mammography alone, and combined USG and mammography for 1 year. Out of a total of 30 cancers detected among these women, USG detected 11 breast cancers and mammography detected five breast cancers, while with combined USG and mammography, 14 patients were diagnosed with breast cancer. Among these 14 cases, all were diagnosed by USG while mammography detected eight cases. This study resulted in greater sensitivity of USG (100%) compared with mammography (57.1%), making ultrasound more sensitive. However, specificity of USG and mammography was 99.9% versus 100% and positive predictive values were 70.0% and 72.7%, respectively [47].

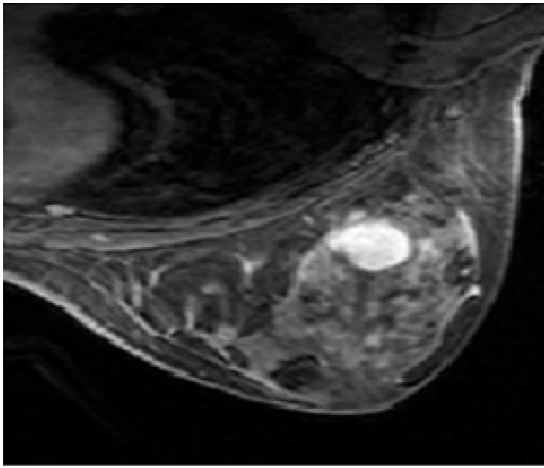
#### 2.5.4. MRI

MRI uses powerful magnetic fields and radio waves to produce field gradients in the form of very detailed, cross-sectional images of the body. It has a sensitivity of 75–100%, specificity of 78–89%, and positive predictive value that ranges from 3% to 33% [48]. Figure 11 shows an MRI picture [49] of an axial contrast-enhanced image of a breast. A nodule with a smooth margin is visible in the breast. The nodule is a fibroadenoma of the breast. Figure 12 shows invasive ductal carcinoma in the right lobe [50].

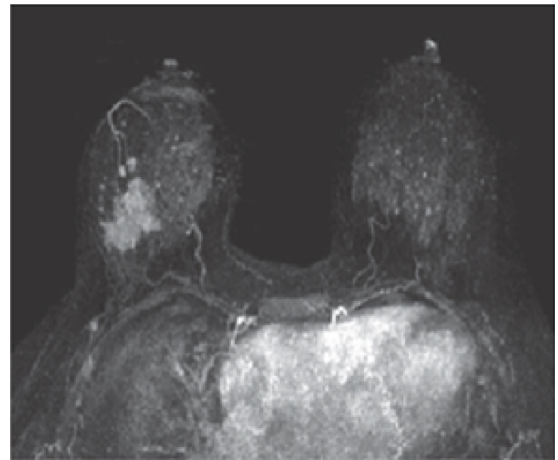
#### 2.5.5. Merits of MRI

The major merits of MRI are as follows. It can image the entire breast in all planes, there is no hazard of ionizing radiation, three-dimensional images, it can detect





**Fig. 11.** The nodule was a fibroadenoma of the breast.



**Fig. 12.** Invasive ductal carcinoma in right breast.

multifocal lesions, it can detect occult lesions and residual malignancy, and it measures the accurate size of lesions with excellent spatial resolution. MRI has a very high negative predictive value in breast lesions. Furthermore, it can image lymph nodes and metastasis and is helpful for staging breast cancer. MRI can identify breast cancer at earlier stage and is excellent among women with BRCA 1 and BRCA 2 positive mutations. MRI has excellent results to evaluate implants.

#### 2.5.6. Demerits of MRI

The major demerits of MRI for its widespread use as a breast cancer screening modality are limited availability, 10-fold higher cost, it needs contrast enhancement and multiple images, and is difficult to interpret. Moreover, false positive results up to 30% in benign lesions, for example in carcinoma *in situ* variable enhancement are reported.

#### 2.5.7. Limitations

There are certain limitations or contraindications for MRI imaging such as gadolinium-based contrast media may lead to allergic conditions and cannot be injected in pregnant women, patients with marked kyphoscoliosis, and who are unable to lie in a prone position.

#### 2.5.8. Recommendations

Worldwide, MRI is not recommended by any country or organization as a primary screening tool for breast cancer screening program for women of any age group. However, it is recommended as an adjunct for screening mammography among women who are at high risk for breast cancer, with a strong family history, BRCA1 or BRCA2 mutation in genes. Use of MRI detected 3.5–28.6 additional breast cancer cases per 1000 examinations (34–86% invasive) and recall rates were 12–24% [48].

The few worldwide recommendations for MRI are as follows. The USPSTF in a recent recommendation published in February 2016 stated that at present, there is insufficient evidence to assess benefits and harms of screening MRI for breast cancer and screening mammography is recommended as the primary screening modality for breast

cancer screening, however, MRI can supplement screening mammography in dense breast and high risk women [17].

The ACS recommended that annual MRI can be added to screening mammography among women who have > 20% lifetime risk of breast cancer [29].

The ACOG did not recommend MRI for average risk women. The college recommended additional MRI for women with > 20% risk of breast cancer and women with BRCA 1 and BRCA 2 positive mutation [30].

#### 2.6. BRCA oncogene mutations

BRCA 1 and BRCA 2 are human tumor suppressor genes present in all humans. These are expressed in breast as well other tissues. Their function is to repair damaged DNA. If these are damaged by BRCA mutations, they are unable to repair damaged DNA. This mutation in BRCA genes increases the risk of breast cancer in affected women. There is 80% risk of breast cancer at the age of 90 years among women with the mutant BRCA1 or BRCA2 gene [52].

Genetic testing for BRCA1 and BRCA2 is not considered a part of the standard workup for breast cancer screening [47], however, the National Cancer Institute stated that women with an abnormal BRCA1 or BRCA2 gene have a 60% risk of being diagnosed with breast cancer disease during their lifetimes, compared to 12–13% for women overall [53].

The recommendations for BRCA carriers are as follows: BSE every month, CBE twice annually, annual mammography, and MRI starting at the age of 25–30 years

### 3. Conclusions

Screening mammography is the most common and widely practiced breast cancer screening modality across the world. The major merits of breast cancer screening programs are: early diagnosis, sorting out and prevention of risk factors, and timely treatment to lessen the morbidity and reduction in 20% of mortality rate. The major demerits of breast cancer screening are overdiagnosis, high cost, ionizing radiation, and their consequences. Worldwide, most

countries recommend biennial screening for breast cancer at 50–74 years of age. However, some countries recommend screening mammography earlier, starting at the age of 40 years until 70–74 years, based on higher breast cancer incidence rate as well as in high risk patients in those countries.

### Conflicts of interest

All contributing authors declare no conflicts of interest.

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