

**American College of Radiology  
ACR Appropriateness Criteria®  
Supplemental Breast Cancer Screening Based on Breast Density**

**Variant 1: Supplemental breast cancer screening. Average-risk females with nondense breasts.**

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
Mammography with IV contrast	Usually Not Appropriate	☼☼
US breast	Usually Not Appropriate	○
MRI breast without and with IV contrast	Usually Not Appropriate	○
MRI breast without and with IV contrast abbreviated	Usually Not Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast abbreviated	Usually Not Appropriate	○
Sestamibi MBI	Usually Not Appropriate	☼☼☼
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼

**Variant 2: Supplemental breast cancer screening. Intermediate-risk females with nondense breasts.**

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
MRI breast without and with IV contrast	May Be Appropriate	○
MRI breast without and with IV contrast abbreviated	May Be Appropriate	○
Mammography with IV contrast	Usually Not Appropriate	☼☼
US breast	Usually Not Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast abbreviated	Usually Not Appropriate	○
Sestamibi MBI	Usually Not Appropriate	☼☼☼
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼

**Variant 3: Supplemental breast cancer screening. High-risk females with nondense breasts.**

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
MRI breast without and with IV contrast	Usually Appropriate	○
Mammography with IV contrast	May Be Appropriate	☼☼
US breast	May Be Appropriate	○
MRI breast without and with IV contrast abbreviated	May Be Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast abbreviated	Usually Not Appropriate	○
Sestamibi MBI	Usually Not Appropriate	☼☼☼
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼

**Variant 4: Supplemental breast cancer screening. Average-risk females with dense breasts.**

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
Mammography with IV contrast	May Be Appropriate	☼☼
US breast	May Be Appropriate (Disagreement)	○
MRI breast without and with IV contrast	May Be Appropriate	○
MRI breast without and with IV contrast abbreviated	May Be Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast abbreviated	Usually Not Appropriate	○
Sestamibi MBI	Usually Not Appropriate	☼☼☼
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼

**Variant 5: Supplemental breast cancer screening. Intermediate-risk females with dense breasts.**

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
Mammography with IV contrast	May Be Appropriate	☼☼
US breast	May Be Appropriate	○
MRI breast without and with IV contrast	May Be Appropriate	○
MRI breast without and with IV contrast abbreviated	May Be Appropriate	○
MRI breast without IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast abbreviated	Usually Not Appropriate	○
Sestamibi MBI	Usually Not Appropriate	☼☼☼
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼

**Variant 6:****Supplemental breast cancer screening. High-risk females with dense breasts.**

Procedure	Appropriateness Category	Relative Radiation Level
US breast	Usually Appropriate	○
Digital breast tomosynthesis screening	Usually Appropriate	☼☼
MRI breast without and with IV contrast	Usually Appropriate	○
MRI breast without and with IV contrast abbreviated	Usually Appropriate	○
Mammography with IV contrast	May Be Appropriate	☼☼
MRI breast without IV contrast	Usually Not Appropriate	○
MRI breast without IV contrast abbreviated	Usually Not Appropriate	○
Sestamibi MBI	Usually Not Appropriate	☼☼☼
FDG-PET breast dedicated	Usually Not Appropriate	☼☼☼☼

## SUPPLEMENTAL BREAST CANCER SCREENING BASED ON BREAST DENSITY

Expert Panel on Breast Imaging: Susan P. Weinstein, MD<sup>a</sup>; Priscilla J. Slanetz, MD, MPH<sup>b</sup>; Alana A. Lewin, MD<sup>c</sup>; Tracy Battaglia, MD, MPH<sup>d</sup>; Anees B. Chagpar, MD, MSc, MPH, MA, MBA<sup>e</sup>; Sandra Dayaratna, MD<sup>f</sup>; Elizabeth H. Dibble, MD<sup>g</sup>; Mita Sanghavi Goel, MD, MPH<sup>h</sup>; Jessica H. Hayward, MD<sup>i</sup>; Charlotte D. Kubicky, MD, PhD<sup>j</sup>; Huong T. Le-Petross, MD<sup>k</sup>; Mary S. Newell, MD<sup>l</sup>; Matthew F. Sanford, MD<sup>m</sup>; John R. Scheel, MD, PhD, MPH<sup>n</sup>; Nina S. Vincoff, MD<sup>o</sup>; Katherine Yao, MD<sup>p</sup>; Linda Moy, MD.<sup>q</sup>

### Summary of Literature Review

#### **Introduction/Background**

Multiple prospective and retrospective studies have demonstrated improved survival and decreased breast cancer mortality with mammographic screening [1-3]. Although mammography remains the only validated screening tool for breast cancer, there are limitations. One of the limitations of mammography is the variable sensitivity based on breast density. The Mammography Quality Standards Act was enacted in 1992 to establish uniform standards in mammographic screening. This led to the development of the ACR BI-RADS<sup>®</sup> Atlas, to clearly and concisely communicate the mammogram results in a standardized format [4]. The BI-RADS<sup>®</sup> Atlas mandates the reporting of breast density in every mammogram report as either fatty, scattered, heterogeneously dense, or extremely dense [4]. The fatty and scattered categories are considered “nondense,” whereas heterogeneously and extremely dense categories are considered “dense.”

Although overall sensitivity of mammography is in the range of 70% to 85%, the sensitivity can vary significantly with breast density [5-7]. The mammographic sensitivity is higher in women with fatty breast parenchyma; however, the sensitivity may decrease to as low as 30% in women with dense breast tissue [5-9]. Although the overall performance of digital mammography is similar to film screen mammography, digital mammography has better performance in specific subgroups, such as in women with dense breasts [8,9]. In addition, even with regular mammographic screening, the interval cancer rate may be as high as 30% [10-13]. Given the limitations of mammography, supplemental screening has been advocated for women with dense breast tissue. In order to bring uniformity to the language, a federal law passed in February 2019, enables the FDA to develop a statement that the effect of breast density on mammographic sensitivity be included in all mammography report.

In women who desire supplemental screening, available options include digital breast tomosynthesis (DBT), whole-breast ultrasound (WBUS), mammography with IV contrast (ie, contrast-enhanced digital mammography [CEDM]), molecular breast imaging (MBI), fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET breast dedicated, MRI breast without intravenous (IV) contrast, MRI breast without and with IV contrast, and abbreviated breast MRI (AB-MRI). Each option has its own benefits and limitations. Similar to 2-D mammography and DBT, WBUS also utilizes morphologic assessment to differentiate the normal parenchyma from benign and suspicious lesions. On the other hand, functional imaging studies utilize neoangiogenesis, vascular permeability, or differential tumor metabolism, which are key features of carcinomas. Functional imaging studies include CEDM, MBI, FDG-PET, MRI breast, and AB-MRI. In this review, we discuss the evidence for supplemental screening by modality based on lifetime risk of breast cancer and breast density. For background material regarding breast cancer screening, the reader should refer to the ACR Appropriateness Criteria<sup>®</sup> topic on “[Breast Cancer Screening](#)” [14]. Women who have <15% lifetime risk are considered to be at average risk, 15% to 20% lifetime risk to be at intermediate risk, and >20% lifetime risk as high risk [15].

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## **Discussion of Procedures by Variant**

### **Variant 1: Supplemental breast cancer screening. Average-risk females with nondense breasts.**

Mammography remains the only validated screening tool for breast cancer screening. Despite widespread mammographic screening, breast cancer represents the leading cause of cancer mortality in women. Although multiple studies have demonstrated improved survival and reduction in breast cancer mortality by up to 30% with regular mammographic screening, there continues to be approximately 40,000 breast cancer deaths annually [10-13]. Women who have <15% lifetime risk are considered to be at average risk [15]. In women with nondense breast tissue, the sensitivity of mammography is high [5].

#### **Digital Breast Tomosynthesis Screening**

DBT allows quasi 3-D images to be reconstructed from the acquired data set, which allows viewing of the reconstructed planar images, thus decreasing the superimposition of normal parenchyma and “unmasking” clinically significant obscured lesions. The addition of DBT to 2-D mammography increases the cancer detection rate (CDR) compared with 2-D mammography alone, resulting in an increase in the CDR, ranging from 1.2/1,000 to 3.0/1,000 [16-20]. Although most studies have reported a statistically significant increase in the CDR with the addition of DBT, some studies have failed to reach a statistical significance [21-23]. In the UK National Health Service TOMosynthesis with digital MammographY (TOMMY) trial, the odds ratio of DBT plus 2-D mammography, compared with 2-D mammography alone, in detecting breast cancer was 1.34; however, this did not reach statistical significance [21,22]. The increase in the CDR has also been demonstrated to be maintained with subsequent screening rounds [17].

In addition to the increase in the CDR, another benefit of adding DBT to 2-D mammography is the reduction in the recall rate [16-19]. In a single-center screening program, Sharpe et al [18] reported a reduction in the recall rate by 18.8%. In the prospective Oslo Tomosynthesis Screening Trial, the recall rate was reduced from 6.7/1,000 to 3.6/1,000 [19]. There is also evidence that the reduction in the recall rate is maintained over consecutive screening episodes [18].

#### **US Breast**

Mammography is the only screening modality proven to decrease breast cancer mortality; however, limited sensitivity of mammography in women with elevated breast density has been in the national spotlight. Currently, national breast density notification legislation is pending, although >75% of the states have currently passed the legislation at the state level. The sensitivity of mammography in fatty breast tissue has been reported to be as high as 98% [5]. In a group of 1,399 women diagnosed with invasive breast carcinoma, Häberle et al [24] assessed the probability of mammography failure based on the breast density. There were 107/1,399 cancers that were only visible on sonography, and the authors found a strong correlation between breast density and mammographic failure. For low-risk women with low breast density, the probability of mammographic failure was 1%, whereas the risk was as high as 40% for high-risk women with dense breast tissue. Chang et al [25] assessed the CDR in average-risk women, and the overall added CDR on sonography was 3.3/1,000, although the added CDR in nondense breasts was 0/1,000.

#### **Mammography With IV Contrast**

CEDM combines the techniques of conventional mammography with administration of IV contrast, thus leveraging functional imaging by assessing for lesion vascularity. A dual-energy technique is utilized to acquire the images in the conventional craniocaudal and mediolateral oblique projections. The acquired data are processed and produce a low-energy image and a diagnostic recombined image. There is limited but emerging literature regarding the use of CEDM in the screening setting [26,27]. However, in the diagnostic setting, CEDM has been shown to demonstrate improved sensitivity and specificity over 2-D mammography [28-31]. The greatest improvement in the sensitivity and specificity is seen in women with dense breast tissue [29,30]. However, at this time there is no relevant literature regarding the use of mammography with IV contrast for supplemental screening in average-risk women with nondense breasts.

#### **MRI Breast Without IV Contrast**

There is no relevant literature regarding the use of MRI breast without IV contrast for supplemental screening in average-risk women with nondense breasts.

#### **MRI Breast Without IV Contrast Abbreviated**

There is no relevant literature regarding the use of AB-MRI breast without IV contrast for supplemental screening in average-risk women with nondense breasts.

### **MRI Breast Without and With IV Contrast Abbreviated**

AB-MRI performed with IV contrast is an abbreviated breast MRI examination. It is similar to a full MRI examination yet does not have a standard protocol; however, at minimum, it must include a precontrast and one postcontrast sequence. A T2-weighted sequence may also be included. There is limited literature supporting the use of AB-MRI breast without and with IV contrast for supplemental screening in average-risk women with nondense breasts. Strahle et al [32] reported on MRI screening on “general unselected female population” utilizing an abbreviated protocol, although the examination consisted of 4 sequences (T2-weighted, precontrast, and 2 postcontrast sequences) in 671 women after negative mammography. In 304/671 women with nondense breasts, no cancers were detected on what the authors defined as AB-MRI [32].

### **MRI Breast Without and With IV Contrast**

There are limited data regarding screening average-risk women with breast MRI with and without IV contrast. In a prospective observational trial, after negative mammographic screening, Kuhl et al [33] reported an additional CDR of 15.5/1,000 with MRI screening in average-risk women across all densities. However, the authors did not analyze the added CDR by breast density.

### **FDG-PET Breast Dedicated**

There is limited relevant literature regarding the use of FDG-PET breast dedicated for supplemental screening in average-risk women with nondense breasts. This is not currently widely used in clinical practice.

### **Sestamibi MBI**

There is limited relevant literature regarding the use of Tc-99m sestamibi MBI for supplemental screening in average-risk women with nondense breasts. This is not currently widely used in clinical practice.

### **Variant 2: Supplemental breast cancer screening. Intermediate-risk females with nondense breasts.**

Women at intermediate risk for breast cancer are defined as having a 15% to 20% lifetime risk [15]. Although there are clear screening guidelines for women with >20% lifetime risk, the screening guidelines have not clearly been defined for women who are at intermediate risk. Women in this category may include patients who have been diagnosed with lobular neoplasia, atypical ductal hyperplasia, previous history of breast cancer, or have a family history of breast cancer without known genetic mutations such as breast cancer gene (BRCA)1/2.

### **Digital Breast Tomosynthesis Screening**

DBT allows quasi 3-D images to be reconstructed from the acquired data set, which allows viewing of the reconstructed planar images, thus decreasing the superimposition of normal parenchyma and “unmasking” clinically significant obscured lesions. The addition of DBT to 2-D mammography increases the CDR compared with 2-D mammography alone, resulting in an increase in the CDR, ranging from 1.2/1,000 to 3.0/1,000 [16-20]. Although most studies have reported a statistically significant increase in the CDR with the addition of DBT, some studies have failed to reach statistical significance [21-23]. In the UK National Health Service TOMMY trial, the odds ratio of DBT plus 2-D mammography, compared with 2-D mammography alone, in detecting breast cancer was 1.34; however, this did not reach statistical significance [21,22]. The increase in the CDR has also been demonstrated to be maintained with subsequent screening rounds [17].

In addition to the increase in the CDR, another benefit of adding DBT to 2-D mammography is the reduction in the recall rate [16-19]. In a single-center screening program, Sharpe et al [18] reported a reduction in the recall rate by 18.8%. In the prospective Oslo Tomosynthesis Screening Trial, the recall rate was reduced from 6.7/1,000 to 3.6/1,000 [19]. There is also evidence that the reduction in the recall rate is maintained over consecutive screening episodes [18].

### **US Breast**

Mammography is the only screening modality proven to decrease breast cancer mortality; however, limited sensitivity of mammography in women with elevated breast density has been in the national spotlight. Currently, national breast density notification legislation is pending, although >75% of the states have currently passed the legislation at the state level. The sensitivity of mammography in fatty breast tissue has been reported to be as high as 98% [5]. In a group of 1,399 women diagnosed with invasive breast carcinoma, Häberle et al [24] assessed the probability of mammography failure based on the breast density. Only 107/1,399 cancers were visible on sonography, and the authors found a strong correlation between breast density and mammographic failure. For low-risk women with low breast density, the probability of mammographic failure was 1%, whereas the risk was as high as 40% for high-risk women with dense breast tissue.

In women with a personal history of breast cancer, the supplemental CDR of screening ultrasound (US) has been reported to be 2.88/1,000 [34]. There was no difference in the CDR based on breast density or age. However, the authors reported an interval cancer rate of 1.5/1,000, which was higher in women who were <50 years of age and in those with dense breast tissue, indicating the failure of screening US in these 2 subgroups.

Cortesi et al [35] evaluated the efficacy of biennial screening US examination in women who were BRCA mutation carriers, high-risk (non-BRCA1/2), and intermediate-risk patients. Overall, MRI had sensitivity of 93.7%, followed by mammography with sensitivity of 55.0% and US with 29.4% sensitivity. In the nondense breast, the sensitivity of mammography was 82.5% versus 10% for US. In the dense breast, the sensitivity of mammography was 50% versus 42.6% for US. Sensitivity analysis by risk level was also performed. The US sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 22.7%, 24.5%, and 33.6%, respectively. The mammographic sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 25.0%, 66.4%, and 56.6%, respectively. Only the BRCA1/2 mutation carriers underwent MRI screening, which demonstrated a sensitivity of 93.7%. The authors did not analyze the efficacy of US screening based on both density and risk.

### **Mammography With IV Contrast**

CEDM combines the techniques of conventional mammography with administration of IV contrast, thus leveraging functional imaging by assessing for lesion vascularity. A dual-energy technique is used to acquire the images in the conventional craniocaudal and mediolateral oblique projections. The acquired data are processed, producing a low-energy image and a diagnostic recombined image. There is limited but emerging literature regarding the use of CEDM in the screening setting. However, in the diagnostic setting, CEDM has been shown to demonstrate improved sensitivity and specificity over 2-D mammography [28-31]. The greatest improvement in the sensitivity and specificity is seen in women with dense breast tissue [29,30]. However, at this time, there is no relevant literature regarding the use of mammography with IV contrast for supplemental screening in intermediate-risk women with nondense breasts.

### **MRI Breast Without IV Contrast Abbreviated**

There is no relevant literature regarding the use of AB-MRI breast without IV contrast for supplemental screening in intermediate-risk women with nondense breasts.

### **MRI Breast Without and With IV Contrast Abbreviated**

AB-MRI performed with IV contrast is an abbreviated breast MRI examination. It is similar to a full MRI examination yet does not have a standard protocol; however, at minimum, it must include a precontrast and one postcontrast sequence. A T2-weighted sequence may also be included. There are currently limited data on screening women with nondense breasts at intermediate lifetime risk with AB-MRI. In 2 retrospective reader studies, in women recently diagnosed with unifocal breast cancer, the sensitivity of AB-MRI was comparable with the full protocol [36,37]. When the performance of AB-MRI was compared with screening US and mammography, there were 12 cancers in 12 women (CDR 15/1,000), 7 of which were not detected on WBUS and mammography [38]. In a prospective observational study of 443 women with mild to moderately elevated lifetime risk for breast cancer, AB-MRI had a similar diagnostic accuracy as the full MRI protocol [39].

### **MRI Breast Without IV Contrast**

There is no relevant literature regarding the use of MRI breast without IV contrast for supplemental screening in intermediate-risk women with nondense breasts.

### **MRI Breast Without and With IV Contrast**

There is some relevant literature supporting the use of MRI breast without and with IV contrast for supplemental screening in intermediate-risk women, specifically in women with a history of lobular carcinoma in situ or a personal history of breast cancer, although these studies included all breast densities [40-42]. At the time of this writing, the American Cancer Society is currently re-reviewing the literature regarding intermediate-risk women; however, its current stance, last updated in 2007, states there is insufficient evidence to formulate a recommendation in this group [15]. As of 2018, ACR recommends annual surveillance MRI in women with dense breasts and a personal history of breast cancer as well as in women who were diagnosed before age 50 [43]. The ACR suggests that MRI should be considered in the following categories: in women with personal histories of breast cancer and who do not fit the 2 previously stated categories and in women with atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ [43].

### **FDG-PET Breast Dedicated**

There is limited relevant literature regarding the use of FDG-PET breast dedicated for supplemental screening in intermediate-risk women with nondense breasts. This is not currently widely used in clinical practice.

### **Sestamibi MBI**

There is limited relevant literature regarding the use of Tc-99m sestamibi MBI for supplemental screening in intermediate-risk women with nondense breasts. This is not currently widely used in clinical practice.

### **Variant 3: Supplemental breast cancer screening. High-risk females with nondense breasts.**

Women with >20% lifetime risk are considered to be at high risk for breast cancer [15]. Regardless of breast density, patients in this category are recommended to begin screening at an earlier age than the average-risk population and to have supplemental screening in addition to mammography. Please refer to the ACR Appropriateness Criteria® topic on “[Breast Cancer Screening](#)” [14] for further guidance.

### **Digital Breast Tomosynthesis Screening**

DBT allows quasi 3-D images to be reconstructed from the acquired data set, which allows viewing of the reconstructed planar images, thus decreasing the superimposition of normal parenchyma and “unmasking” clinically significant obscured lesions. The addition of DBT to 2-D mammography increases the CDR compared with 2-D mammography alone, resulting in an increase in the CDR, ranging from 1.2/1,000 to 3.0/1,000 [16-20]. Although most studies have reported a statistically significant increase in the CDR with the addition of DBT, some studies have failed to reach statistical significance [21-23]. In the UK National Health Service TOMMY trial, the odds ratio of DBT plus 2-D mammography, compared with 2-D mammography alone, in detecting breast cancer was 1.34; however, this did not reach statistical significance [21,22]. The increase in the CDR has also been demonstrated to be maintained with subsequent screening rounds [17].

In addition to the increase in the CDR, another benefit of adding DBT to 2-D mammography is the reduction in the recall rate [16-19]. In a single-center screening program, Sharpe et al [18] reported a reduction in the recall rate by 18.8%. In the prospective Oslo Tomosynthesis Screening Trial, the recall rate was reduced from 6.7/1,000 to 3.6/1,000 [19]. There is also evidence that the reduction in the recall rate is maintained over consecutive screening episodes [18].

### **US Breast**

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Cortesi et al [35] evaluated the efficacy of biannual screening US examination in women who were BRCA mutation carriers, high-risk (non-BRCA1/2), and intermediate-risk patients. Overall, MRI had sensitivity of 93.7%, which was followed by mammography (55.0%), and US (29.4%). In the nondense breast, the sensitivity of mammography was 82.5% versus 10% for US. In the dense breast, the sensitivity of mammography was 50% versus 42.6% for US. Sensitivity analysis by risk level was also performed. The US sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 22.7%, 24.5%, and 33.6%, respectively. The mammographic sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 25.0%, 66.4%, and 56.6%, respectively. Only the BRCA1/2 mutation carriers underwent MRI screening, which demonstrated a sensitivity of 93.7%. The authors did not analyze the efficacy of US screening based on both density and risk.

The addition of WBUS to mammography increases the CDR in high-risk women. In a surveillance cohort study of 529 women with elevated lifetime risk, the sensitivity of mammography, WBUS, and the 2 modalities combined was 33%, 40%, and 49%, respectively [44]. However, subgroup analysis was not performed by breast density. In the same population, MRI had a sensitivity of 91% [44]. In the ACRIN 6666 trial, after 3 rounds of screening mammography and screening WBUS in women with dense breast tissue at intermediate to elevated lifetime risk, the sensitivity, specificity, and positive predictive value (PPV3) of mammography was 0.52, 0.91, and 0.38,



respectively. The addition of US to mammography increased the sensitivity (0.76) but decreased the specificity (0.84) and the PPV3 (0.38) [45]. In a prospective cohort trial of 687 high-risk women, the cancer yield of mammography alone was 5.4/1,000 and increased to 7.7/1,000 with the addition of US [46].

### **Mammography With IV Contrast**

CEDM combines the techniques of conventional mammography with administration of IV contrast, thus leveraging functional imaging by assessing for lesion vascularity. A dual-energy technique is utilized to acquire the images in the conventional craniocaudal and mediolateral oblique projections. The acquired data are processed, producing a low-energy image and a diagnostic recombined image. There is limited literature regarding the use of CEDM in the screening setting. However, in the diagnostic setting, CEDM has been shown to demonstrate improved sensitivity and specificity over 2-D mammography [28-31]. The greatest improvement in the sensitivity and specificity is seen in women with dense breast tissue [29,30]. At this time, there is limited but emerging literature regarding the use of mammography with IV contrast for supplemental screening in high-risk women with nondense breasts. Jochelson et al [47] screened 318 high-risk women using both CEDM and MRI [47]. Both techniques detected carcinomas not visualized on mammography, 2 using CEDM and 3 using MRI.

### **MRI Breast Without IV Contrast Abbreviated**

There is no relevant literature regarding the use of AB-MRI breast without IV contrast for supplemental screening in high-risk women with nondense breasts.

### **MRI Breast Without and With IV Contrast Abbreviated**

AB-MRI performed with IV contrast is an abbreviated breast MRI examination. It is similar to a full MRI examination yet does not have a standard protocol; however, at minimum, it must include a precontrast and one postcontrast sequence. A T2-weighted sequence may also be included. There is limited relevant literature regarding the use of AB-MRI breast without and with IV contrast in high-risk women with nondense breasts. In 2 retrospective studies comparing the full diagnostic protocol with an abbreviated protocol in high-risk women, the authors found both protocols to have similar sensitivity [48,49]. However, neither study evaluated the CDR by breast density.

### **MRI Breast Without IV Contrast**

There is no relevant literature regarding the use of MRI breast without IV contrast for supplemental screening in high-risk women with nondense breasts.

### **MRI Breast Without and With IV Contrast**

The American Cancer Society and ACR advocate MRI screening in high-risk women regardless of breast density [15,43]. There is ample evidence in the literature supporting this recommendation [46,50-54]. In the high-risk population, sensitivity of mammography alone is approximately 31% to 33% compared with the sensitivity of MRI alone (87%–96%) [45,46,55]. The combination of mammography and MRI yields 100% sensitivity compared with the 44% to 48% sensitivity of combined mammography and US [45,46]. In addition, the types of carcinoma detected on MRI compared with mammography may differ. Cancers detected on MRI are more likely to be invasive carcinomas (71%), whereas cancers detected on mammography are more likely to be either ductal carcinoma in situ (65%) or associated with calcifications (88%) [56].

### **FDG-PET Breast Dedicated**

There is limited relevant literature regarding the use of FDG-PET breast dedicated for supplemental screening in high-risk women with nondense breasts. This is not currently widely used in clinical practice.

### **Sestamibi MBI**

There is limited relevant literature regarding the use of Tc-99m sestamibi MBI for supplemental screening in high-risk women with nondense breasts. This is not currently widely used in clinical practice.

### **Variant 4: Supplemental breast cancer screening. Average-risk females with dense breasts.**

Mammography remains the only validated screening tool for breast cancer screening. Despite widespread mammographic screening, breast cancer represents the leading cause of cancer mortality in women. Although multiple studies have demonstrated improved survival and reduction in breast cancer mortality by up to 30% with regular mammographic screening, there continues to be approximately 40,000 breast cancer deaths annually [10-13]. Women who have <15% lifetime risk are considered to be at average risk [15].

## Digital Breast Tomosynthesis Screening

DBT allows quasi 3-D images to be reconstructed from the acquired data set, which allows viewing of reconstructed planar images, thus decreasing the superimposition of normal parenchyma and “unmasking” clinically significant obscured lesions. The addition of DBT to 2-D mammography increases the CDR compared with 2-D mammography alone, resulting in an increase in the CDR, ranging from 1.2/1,000 to 3.0/1,000 [16-20]. Although most studies have reported a statistically significant increase in the CDR with the addition of DBT, some studies have failed to reach statistical significance [21-23]. In the UK National Health Service TOMMY trial, the odds ratio of DBT plus 2-D mammography, compared with 2-D mammography alone, in detecting breast cancer was 1.34; however, this did not reach statistical significance [21,22]. The increase in the CDR has also been demonstrated to be maintained with subsequent screening rounds [17].

The greatest improvement in the CDR with DBT is seen in women with dense breast tissue [21,22,57,58]. Although the TOMMY trial did not reach statistical significance across all breast densities, in women with >50% breast density, statistical significance was achieved with the sensitivity of 2-D mammography plus DBT reaching 93% versus 86% for 2-D mammography alone [21,22]. In a meta-analysis of 16 studies evaluating women with dense breasts, addition of DBT improved the CDR, compared with 2-D mammography alone, in both diagnostic (relative risk [RR]: 1.16) and the screening (RR: 1.33) settings [58].

In addition to the increase in the CDR, another benefit of adding DBT to 2-D mammography is the reduction in the recall rate [16-19]. In a single-center screening program, Sharpe et al [18] reported a reduction in the recall rate by 18.8%. In the prospective Oslo Tomosynthesis Screening Trial, the recall rate was reduced from 6.7/1,000 to 3.6/1,000 [19]. There is also evidence that the reduction in the recall rate is maintained over consecutive screening episodes [18].

## US Breast

Mammography is the only screening modality proven to decrease breast cancer mortality; however, limited sensitivity of mammography in women with elevated breast density has been in the national spotlight. Currently, national breast density notification legislation is pending, although >75% of the states have currently passed the legislation at the state level. The sensitivity of mammography in fatty breast tissue has been reported to be as high as 98% [5]. In a group of 1,399 women diagnosed with invasive breast carcinoma, Häberle et al [24] assessed the probability of mammography failure based on the breast density. Only 107/1399 cancers were visible on sonography, and the authors found a strong correlation between breast density and mammographic failure. For low-risk women with low breast density, the probability of mammographic failure was 1%, whereas the risk was as high as 40% for high-risk women with dense breast tissue. Chang et al [25] assessed the CDR in average-risk women, and the overall added CDR on sonography was 3.3/1,000, although the added CDR in nondense breasts was 0/1,000. However, the rise in the CDR with WBUS was associated with a decreased PPV2 and an increased BI-RADS® category 3 rate.

At a high-volume screening center, when women with heterogeneously or extremely dense breast tissue were offered automated 3-D US screening in addition to full-field digital mammography (FFDM), the added CDR rose by 2.4/1,000 screened (6.6/1,000 automated 3-D US screening plus FFDM versus 4.2/1,000 for FFDM alone) [59]. However, the risk level of the population was not defined other than patients with a personal history of breast cancer were excluded, and 3.5% of the patients reported a family history of breast cancer.

Buchberger et al [60] compared the performance of screening mammography with and without screening US in average-risk women. In the subgroup of women with dense breasts, the CDR increased from 1.8/1,000 to 2.4/1,000, with the addition of screening US. However, the PPV2 decreased from 52.7/1,000 with mammography alone to 37.7/1,000 with mammography plus US. For the entire population, there were 28 interval cancer rates within a 12-month period after screening (0.42/1,000): 18 in women with dense breasts and 10 in women with nondense breasts.

In the Japan Strategic Anti-cancer Randomized Trial, 72,998 asymptomatic women 40 to 49 years of age were randomized to mammographic screening alone or mammographic plus US screening [61]. The sensitivity and specificity in the mammogram arm were 77.0% and 91.4%, respectively. In comparison, the mammogram plus US arm had a higher sensitivity (91.1%) but lower specificity (87.7%). The interval cancer rate was halved in the arm that received US screening, from the baseline level of 0.10% to 0.05%.

Using Breast Cancer Surveillance Consortium data, Lee et al [62] assessed the performance of the addition of screening US in women with dense breasts in the community. The CDR of mammography plus US was 5.4/1,000 versus 5.5/1,000 for mammography alone. The false-positive biopsy rate and PPV of biopsy recommendations for

mammography plus US were 52.0/1,000 and 9.5%, respectively, compared with 22.2/1,000 and 21.4%, respectively, for mammography alone. The interval cancer rate did not differ significantly in the 2 arms: the mammography plus US arm was 1.5/1,000 versus 1.9/1,000 for mammography alone. Utilizing the registry data and data from the literature, Sprague et al [63] used simulation models to assess the outcomes of supplemental US screening after negative screening mammography in women with dense breasts. Per 1,000 women screened, the authors concluded there would be 0.36 breast cancer deaths averted, 354 additional biopsy recommendations, and 1.7 quality-adjusted life-years gained at a cost \$325,000 for each quality-adjusted life-year gained [63].

Although the supplemental screening debate was initiated partly because of the limitations of screening mammography in women with dense breast tissue, there is some evidence to suggest that breast density alone may not be sufficient reason to recommend supplemental screening. One way to assess the failure of mammography is by determining the interval cancer rate in the study population. Using the Breast Cancer Surveillance Consortium data, the women most likely to present with interval cancers were women with an elevated 5-year risk for breast cancer >1.67% and with dense breast tissue, representing approximately 24% of all women with dense breasts [64].

### **Mammography With IV Contrast**

CEDM combines the techniques of conventional mammography with administration of IV contrast, thus leveraging functional imaging by assessing for lesion vascularity. A dual-energy technique is used to acquire the images in the conventional craniocaudal and mediolateral oblique projections. The acquired data are processed, producing a low-energy image and a diagnostic recombined image. There is limited but emerging literature regarding the use of CEDM in the screening setting. However, in the diagnostic setting, CEDM has been shown to demonstrate improved sensitivity and specificity over 2-D mammography [28-31]. The greatest improvement in the sensitivity and specificity is seen in women with dense breast tissue [29,30]. At this time, there is limited literature regarding the use of mammography with IV contrast for supplemental screening in average-risk women with dense breasts.

### **MRI Breast Without IV Contrast Abbreviated**

There is no relevant literature regarding the use of AB-MRI breast without IV contrast for supplemental screening in average-risk women with dense breasts.

### **MRI Breast Without and With IV Contrast Abbreviated**

AB-MRI performed with IV contrast is an abbreviated breast MRI examination. It is similar to a full MRI examination yet does not have a standard protocol; however, at minimum, it must include a precontrast and one postcontrast sequence. A T2-weighted sequence may also be included. There is limited literature supporting the use of AB-MRI breast without and with IV contrast for supplemental screening in average-risk women with dense breasts. Strahle et al [32] reported an additional CDR of 16.3/1,000 using an “abbreviated protocol” consisting of 4 sequences (T2-weighted, precontrast, and 2 postcontrast sequences) in 367 women with dense breasts after negative mammography. Chen et al [65] found no significant difference in sensitivity between a full breast MRI protocol and an abbreviated protocol in 478 women with dense breast tissue and with no significant family history of breast cancer. In a prospective multi-institutional ECOG-ACRIN trial, EA1141, comparing the diagnostic performance of AB-MRI and DBT in average-risk women with dense breasts, the CDR for invasive cancer with DBT was 4.8/1,000 and 11.8/1,000 with AB-MRI. The incremental difference in the CDR between the 2 modalities was 7/1,000, or a difference of 245% [66].

### **MRI Breast Without IV Contrast**

There is no relevant literature regarding the use of MRI breast without IV contrast for supplemental screening in average-risk women with dense breasts.

### **MRI Breast Without and With IV Contrast**

There are limited data regarding screening average-risk women with breast MRI with and without IV contrast. In a prospective observational trial, after negative mammographic screening, Kuhl et al [33] reported an additional CDR of 15.5/1,000 with MRI screening in average-risk women across all densities. However, the authors did not analyze the added CDR by breast density.

### **FDG-PET Breast Dedicated**

There is limited relevant literature regarding the use of FDG-PET breast dedicated for supplemental screening in average-risk women with dense breasts [67]. This is not currently widely used in clinical practice.

## **Sestamibi MBI**

There is limited relevant literature regarding the use of Tc-99m sestamibi MBI for supplemental screening in average-risk women with dense breasts. This is not currently widely used in clinical practice.

There are reports of supplemental cancer detection (7.7–8.8/1,000) with MBI after negative mammography in women with dense breast tissue, but the data are limited [68-70].

### **Variant 5: Supplemental breast cancer screening. Intermediate-risk females with dense breasts.**

Women at intermediate risk for breast cancer are defined as having a 15% to 20% lifetime risk [15]. Although there are clear screening guidelines for women with >20% lifetime risk, the screening guidelines have not been clearly defined for women who are at intermediate risk. Women in this category may include patients who have been diagnosed with lobular neoplasia, atypical ductal hyperplasia, previous history of breast cancer, or have a family history of breast cancer without known genetic mutations such as BRCA1/2.

## **Digital Breast Tomosynthesis Screening**

DBT allows quasi 3-D images to be reconstructed from the acquired data set, allowing for viewing of the reconstructed planar images, thus decreasing the superimposition of normal parenchyma and “unmasking” clinically significant obscured lesions. The addition of DBT to 2-D mammography increases the CDR compared with use of 2-D mammography alone, resulting in an increase in the CDR, ranging from 1.2/1,000 to 3.0/1,000 [16-20]. Although most studies have reported a statistically significant increase in the CDR with the addition of DBT, some studies have failed to reach statistical significance [21-23]. In the UK National Health Service TOMMY trial, the odds ratio of DBT plus 2-D mammography, compared with 2-D mammography alone, in detecting breast cancer was 1.34; however, this did not reach statistical significance [21,22]. The increase in the CDR has also been demonstrated to be maintained with subsequent screening rounds [17].

The greatest improvement in the CDR with DBT is seen in women with dense breast tissue [21,22,57,58]. Although the TOMMY trial did not reach statistical significance across all breast densities, in women with >50% breast density, statistical significance was achieved with the sensitivity of 2-D mammography plus DBT reaching 93% versus 86% for 2-D mammography alone [21,22]. In a meta-analysis of 16 studies evaluating women with dense breasts, DBT improved the CDR compared with 2-D mammography alone, in both the diagnostic (RR: 1.16) and the screening (RR: 1.33) settings [58].

In addition to the increase in the CDR, another benefit of adding DBT to 2-D mammography is the reduction in the recall rate [16-19]. In a single-center screening program, Sharpe et al [18] reported a reduction in the recall rate by 18.8%. In the prospective Oslo Tomosynthesis Screening Trial, the recall rate was reduced from 6.7/1,000 to 3.6/1,000 [19]. There is also evidence that the reduction in the recall rate is maintained over consecutive screening episodes [18].

## **US Breast**

Mammography is the only screening modality proven to decrease breast cancer mortality; however, limited sensitivity of mammography in women with elevated breast density has been in the national spotlight. Currently, national breast density notification legislation is pending, although >75% of the states have currently passed the legislation at the state level. The sensitivity of mammography in fatty breast tissue has been reported to be as high as 98% [5]. In a group of 1,399 women diagnosed with invasive breast carcinoma, Häberle et al [24] assessed the probability of mammography failure based on the breast density. Only 107/1,399 cancers were visible on sonography, and the authors found a strong correlation between breast density and mammographic failure. For low-risk women with low breast density, the probability of mammographic failure was 1%, whereas the risk was as high as 40% for high-risk women with dense breast tissue.

In women with a personal history of breast cancer, the supplemental CDR of screening US has been reported to be 2.88/1,000 [34]. There was no difference in the CDR based on breast density or age. However, the authors reported an interval cancer rate of 1.5/1,000, which was higher in women who were <50 years of age and in those with dense breast tissue, indicating the failure of screening US in the 2 subgroups.

Cortesi et al [35] evaluated the efficacy of biannual screening US examination in women who were BRCA mutation carriers, high-risk (non-BRCA1/2), and intermediate-risk patients. Overall, MRI had sensitivity of 93.7%, followed by mammography (55.0%) and US (29.4%). In the nondense breast, the sensitivity of mammography was 82.5% versus 10% for US. In the dense breast, the sensitivity of mammography was 50% versus 42.6% for US. Sensitivity analysis by risk level was also performed. The US sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and

intermediate-risk patients were 22.7%, 24.5%, and 33.6%, respectively. The mammographic sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 25.0%, 66.4%, and 56.6%, respectively. Only the BRCA1/2 mutation carriers underwent MRI screening, which demonstrated a sensitivity of 93.7%. The authors did not analyze the efficacy of US screening based on both density and risk.

Although the supplemental screening debate was initiated partly because of the limitations of screening mammography in women with dense breast tissue, there is some evidence to suggest that breast density alone may not be sufficient reason to recommend supplemental screening. One way to assess the failure of mammography is by determining the interval cancer rate in the study population. Using Breast Cancer Surveillance Consortium data, the women most likely to present with interval cancers were women with an elevated 5-year risk for breast cancer >1.67% and with dense breast tissue, representing approximately 24% of all women with dense breasts [64].

### **Mammography With IV Contrast**

CEDM combines the techniques of conventional mammography with administration of IV contrast, thus leveraging functional imaging by assessing for lesion vascularity. A dual-energy technique is utilized to acquire the images in the conventional craniocaudal and mediolateral oblique projections. The acquired data are processed, producing a low-energy image and a diagnostic recombined image. There is limited literature regarding the use of CEDM in the screening setting. However, in the diagnostic setting, CEDM has been shown to demonstrate improved sensitivity and specificity over 2-D mammography [28-31]. The greatest improvement in the sensitivity and specificity is seen in women with dense breast tissue [29,30]. At this time, there is limited but emerging literature regarding the use of mammography with IV contrast for supplemental screening in intermediate-risk women with dense breasts. However, in women with dense breast tissue and given the limited sensitivity of mammography and the need for supplemental screening, CEDM may have a potential role; however, more data on CEDM in the screening setting in intermediate-risk women with dense breast tissue are needed.

### **MRI Breast Without IV Contrast Abbreviated**

There is no relevant literature regarding the use of AB-MRI breast without IV contrast for supplemental screening in intermediate-risk women with dense breasts.

### **MRI Breast Without and With IV Contrast Abbreviated**

AB-MRI performed with IV contrast is an abbreviated breast MRI examination. It is similar to a full MRI examination yet does not have a standard protocol; however, at minimum, it must include a precontrast and one postcontrast sequence. A T2-weighted sequence may also be included. There are currently limited data on screening women with dense breasts at intermediate lifetime risk with AB-MRI. In 2 retrospective reader studies, in women recently diagnosed with unifocal breast cancer, the sensitivity of AB-MRI was comparable with the full protocol [36,37]. When the performance of AB-MRI was compared with screening US and mammography, 12 cancers in 12 women (CDR 15/1,000) were detected, 7 of which were not detected on WBUS and mammography [38]. In a prospective observational study of 443 women with mild to moderately elevated lifetime risk for breast cancer, AB-MRI had a similar diagnostic accuracy as the full MRI protocol [39].

### **MRI Breast Without IV Contrast**

There is no relevant literature regarding the use of MRI breast without IV contrast for supplemental screening in intermediate-risk women with dense breasts.

### **MRI Breast Without and With IV Contrast**

There is some relevant literature supporting the use of MRI breast without and with IV contrast for supplemental screening in intermediate-risk women, specifically in women with a history of lobular carcinoma in situ or a personal history of breast cancer, although these studies included all breast densities [40-42]. At the time of this writing, the American Cancer Society was re-reviewing the literature regarding intermediate-risk women; however, its current stance, last updated in 2007, states there is insufficient evidence to formulate a recommendation in this group [15]. As of 2018, the ACR recommends annual surveillance MRI in women with dense breasts and with a personal history of breast cancer, as well as in women who were diagnosed before age 50 [43]. The ACR suggests that MRI should be considered in the following categories: in women with personal histories of breast cancer and who do not fit the 2 previously stated categories as well as in women with atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ [43].

### **FDG-PET Breast Dedicated**

There is limited relevant literature regarding the use of FDG-PET breast dedicated for supplemental screening in intermediate-risk women with dense breasts. This is not currently widely used in clinical practice.

## Sestamibi MBI

There is limited relevant literature regarding the use of Tc-99m sestamibi MBI for supplemental screening in intermediate-risk women with dense breasts. This is not currently widely used in clinical practice.

### **Variant 6: Supplemental breast cancer screening. High-risk females with dense breasts.**

Women with >20% lifetime risk are considered to be at high risk for breast cancer [15]. Regardless of breast density, patients in this category are recommended to begin screening at an earlier age than the average-risk population and to have supplemental screening in addition to mammography. Please refer to the ACR Appropriateness Criteria® topic titled “[Breast Cancer Screening](#)” [14] for further guidance.

### **Digital Breast Tomosynthesis Screening**

DBT allows quasi 3-D images to be reconstructed from the acquired data set, which allows for viewing of the reconstructed planar images, thus decreasing the superimposition of normal parenchyma and “unmasking” clinically significant obscured lesions. The addition of DBT to 2-D mammography increases the CDR compared with 2-D mammography alone, resulting in an increase in the CDR, ranging from 1.2/1,000 to 3.0/1,000 [16-20]. Although most studies have reported a statistically significant increase in the CDR with the addition of DBT, some studies have failed to reach statistical significance [21-23]. In the UK National Health Service TOMMY trial, the odds ratio of DBT plus 2-D mammography, compared with 2-D mammography alone, in detecting breast cancer was 1.34; however, this did not reach statistical significance [21,22]. The increase in the CDR has also been demonstrated to be maintained with subsequent screening rounds [17].

The greatest improvement in the CDR with DBT is seen in women with dense breast tissue [21,22,57,58]. Although the TOMMY trial did not reach statistical significance across all breast densities, in women with >50% breast density, statistical significance was achieved, with the sensitivity of 2-D mammography plus DBT reaching 93% versus 86% for 2-D mammography alone [21,22]. In a meta-analysis of 16 studies evaluating women with dense breasts, DBT improved the CDR compared with 2-D mammography alone in both the diagnostic (RR: 1.16) and the screening (RR: 1.33) settings [58].

In addition to the increase in the CDR, another benefit of adding DBT to 2-D mammography is the reduction in the recall rate [16-19]. In a single-center screening program, Sharpe et al [18] reported a reduction in the recall rate by 18.8%. In the prospective Oslo Tomosynthesis Screening Trial, the recall rate was reduced from 6.7/1,000 to 3.6/1,000 [19]. There is also evidence that the reduction in the recall rate is maintained over consecutive screening episodes [18].

### **US Breast**

Mammography is the only screening modality proven to decrease breast cancer mortality; however, limited sensitivity of mammography in women with elevated breast density has been in the national spotlight. Currently, national breast density notification legislation is pending, although >75% of the states have currently passed the legislation at the state level. The sensitivity of mammography in fatty breast tissue has been reported to be as high as 98% [5]. In a group of 1,399 women diagnosed with invasive breast carcinoma, Häberle et al [24] assessed the probability of mammography failure based on the breast density. Only 107/1,399 cancers were visible on sonography, and the authors found a strong correlation between breast density and mammographic failure. For low-risk women with low breast density, the probability of mammographic failure was 1%, whereas the risk was as high as 40% for high-risk women with dense breast tissue.

Cortesi et al [35] evaluated the efficacy of biannual screening US examination in women who were BRCA mutation carriers, high-risk (non-BRCA1/2), and intermediate-risk patients. Overall, MRI had sensitivity of (93.7%), followed by mammography (55.0%), then US (29.4%). In the nondense breast, the sensitivity of mammography was 82.5% versus 10% for US. In the dense breast, the sensitivity of mammography was 50% versus 42.6% for US. Sensitivity analysis by risk level was also performed. The US sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 22.7%, 24.5%, and 33.6%, respectively. The mammographic sensitivities for BRCA1/2, high-risk (non-BRCA1/2), and intermediate-risk patients were 25.0%, 66.4%, and 56.6%, respectively. Only the BRCA1/2 mutation carriers underwent MRI screening, which demonstrated a sensitivity of 93.7%. The authors did not analyze the efficacy of US screening based on both density and risk.

The addition of WBUS to mammography increases the CDR in high-risk women. In a surveillance cohort study of 529 women with elevated lifetime risk, the sensitivity of mammography, WBUS, and the 2 modalities combined was 33%, 40%, and 49%, respectively [44]. However, subgroup analysis was not performed by breast density. In

the same population, MRI had a sensitivity of 91% [44]. In the ACIN 6666 trial, after 3 rounds of screening mammography and screening WBUS in women with dense breast tissue at intermediate to elevated lifetime risk, the sensitivity, specificity, and PPV3 of mammography was 0.52, 0.91, and 0.38, respectively. The addition of US to mammography increased the sensitivity (0.76) but decreased the specificity (0.84) and PPV3 (0.38) [45]. In a prospective cohort trial of 687 high-risk women, the cancer yield of mammography alone was 5.4/1,000 and increased to 7.7/1,000 with the addition of US [46].

### **Mammography With IV Contrast**

CEDM combines the techniques of conventional mammography with administration of IV contrast, thus leveraging functional imaging by assessing for lesion vascularity. A dual-energy technique is used to acquire the images in the conventional craniocaudal and mediolateral oblique projections. The acquired data are processed, producing a low-energy image and a diagnostic recombined image. There is limited but emerging literature regarding the use of CEDM in the screening setting. However, in the diagnostic setting, CEDM has been shown to demonstrate improved sensitivity and specificity over 2-D mammography [28-31]. The greatest improvement in the sensitivity and specificity is seen in women with dense breast tissue [29,30]. Jochelson et al [47] screened 318 high-risk women using both CEDM and MRI [47]. Both techniques detected carcinomas not visualized on mammography—two on CEDM and 3 on MRI—and the authors feel there is a potential role of CEDM in patients, although a subanalysis based on breast density was not performed. At this time, there is limited literature assessing the use of mammography with IV contrast for supplemental screening in high-risk women with dense breasts.

### **MRI Breast Without IV Contrast Abbreviated**

There is no relevant literature regarding the use of AB-MRI breast without IV contrast for supplemental screening in high-risk women with dense breasts.

### **MRI Breast Without and With IV Contrast Abbreviated**

AB-MRI performed with IV contrast is an abbreviated breast MRI examination. It is similar to a full MRI examination yet does not have a standard protocol; however, at minimum, it must include a precontrast and one postcontrast sequence. A T2-weighted sequence may also be included. There is limited relevant literature regarding the use of AB-MRI breast without and with IV contrast in high-risk women with dense breasts. In 2 retrospective studies comparing the full diagnostic protocol to an abbreviated protocol in high-risk women, the authors found both protocols to have similar sensitivity [48,49]. However, neither study evaluated the CDR by breast density.

### **MRI Breast Without IV Contrast**

There is no relevant literature regarding the use of MRI breast without IV contrast for supplemental screening in high-risk women with dense breasts.

### **MRI Breast Without and With IV Contrast**

The American Cancer Society advocates MRI screening in high-risk women regardless of breast density [15]. There is ample evidence in the literature supporting this recommendation [46,50-54]. In the high-risk population, sensitivity of mammography alone is approximately 31% to 33%, compared with the sensitivity of MRI alone which is 87% to 96% [45,46,55]. The combination of mammography and MRI yields 100% sensitivity compared with the 44% to 48% sensitivity of combined mammography and US [45,46]. In addition, the types of carcinoma detected on MRI compared with mammography may differ. Cancers detected on MRI are more likely to be invasive carcinomas (71%), whereas cancers detected on mammography were are likely to be ductal carcinoma in situ (65%), or associated with calcifications (88%) [56].

### **FDG-PET Breast Dedicated**

There is limited relevant literature regarding the use of FDG-PET breast dedicated for supplemental screening in high-risk women with dense breasts. This is not currently widely used in clinical practice.

### **Sestamibi MBI**

There is limited relevant literature regarding the use of Tc-99m sestamibi MBI for supplemental screening in high-risk women with dense breasts. This is not currently widely used in clinical practice.

### **Summary of Recommendations**

- **Variant 1:** DBT screening is usually appropriate as the supplemental breast cancer screening of average-risk females with nondense breasts.

- **Variation 2:** DBT screening is usually appropriate as the supplemental breast cancer screening of intermediate-risk females with nondense breasts.
- **Variation 3:** DBT screening and MRI breast without and with IV contrast is usually appropriate for supplemental breast cancer screening of high-risk females with nondense breasts. These procedures are complementary (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient’s care).
- **Variation 4:** DBT screening is usually appropriate as the supplemental breast cancer screening of average-risk females with dense breasts. The panel did not agree on recommending US breast for patients in this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from this procedure. Imaging with US breast is controversial but may be appropriate.
- **Variation 5:** DBT screening is usually appropriate for supplemental breast cancer screening of intermediate-risk females with dense breasts.
- **Variation 6:** DBT screening and MRI breast without and with IV contrast are usually appropriate for supplemental breast cancer screening of high-risk females with dense breasts. These procedures are complementary (ie, more than one procedure is ordered as a set or simultaneously wherein each procedure provides unique clinical information to effectively manage the patient’s care). MRI breast without and with IV contrast abbreviated and US breast are alternatives to MRI breast without and with IV contrast (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient’s care), but MRI has the highest sensitivity for breast cancer detection.

### Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to [www.acr.org/ac](http://www.acr.org/ac).

### Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel’s recommendation. “May be appropriate” is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with



different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document [71].

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
○	0 mSv	0 mSv
⊕	<0.1 mSv	<0.03 mSv
⊕⊕	0.1-1 mSv	0.03-0.3 mSv
⊕⊕⊕	1-10 mSv	0.3-3 mSv
⊕⊕⊕⊕	10-30 mSv	3-10 mSv
⊕⊕⊕⊕⊕	30-100 mSv	10-30 mSv

\*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies.”

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.