NCCN Continuing Education

Target Audience: This activity is designed to meet the educational needs of oncologists, nurses, pharmacists, and other healthcare professionals who manage patients with cancer.

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Release date: September 10, 2023; Expiration date: September 10, 2024

Learning Objectives:

Upon completion of this activity, participants will be able to:

- Integrate into professional practice the updates to the NCCN Guidelines for Breast Cancer Screening and Diagnosis
- Describe the rationale behind the decision-making process for developing the NCCN Guidelines for Breast Cancer Screening and Diagnosis

Disclosure of Relevant Financial Relationships

None of the planners for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients.

Individuals Who Provided Content Development and/or Authorship Assistance:

The faculty listed below have no relevant financial relationship(s) with ineligible companies to disclose.

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Therese B. Bevers, MD, Panel Chair, has disclosed receiving grant/research support from Namida Lab, Inc., Preferred Medicine, and Toray Industries, Inc.
Bethany L. Niell, MD, PhD, Panel Vice Chair, has disclosed receiving grant/research support from Hologic, Inc.
Emily F. Conant, MD, Panel Member, has disclosed receiving grant/research support from iCAD Inc. and OM1, Inc.; and serving as a scientific advisor for iCAD Inc.
Roberta M. Strigel, MD, MS, Panel Member, has disclosed receiving grant/research support from General Electric.

To view all of the conflicts of interest for the NCCN Guidelines panel, go to NCCN.org/guidelines/guidelines-panels-and-disclosure/disclosure-panels

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Breast Cancer Screening and Diagnosis, Version 1.2023

Featured Updates to the NCCN Guidelines

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ABSTRACT

The NCCN Guidelines for Breast Cancer Screening and Diagnosis provide health care providers with a practical, consistent framework for screening and evaluating a spectrum of clinical presentations and breast lesions. The NCCN Breast Cancer Screening and Diagnosis Panel is composed of a multidisciplinary team of experts in the field, including representation from medical oncology, gynecologic oncology, surgical oncology, internal medicine, family practice, preventive medicine, pathology, diagnostic and interventional radiology, as well as patient advocacy. The NCCN Breast Cancer Screening and Diagnosis Panel meets at least annually to review emerging data and comments from reviewers within their institutions to guide updates to existing recommendations. These NCCN Guidelines Insights summarize the panel's decision-making and discussion surrounding the most recent updates to the guideline's screening recommendations.

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*Provided content development and/or authorship assistance.

NCCN CATEGORIES OF EVIDENCE AND CONSENSUS

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

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All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

PLEASE NOTE

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. **The NCCN Guidelines Insights highlight important changes in the NCCN Guidelines recommendations from previous versions. Colored markings in the algorithm show changes and the discussion aims to further the understanding of these changes by summarizing salient portions of the panel's discussion, including the literature reviewed.**

The NCCN Guidelines Insights do not represent the full NCCN Guidelines; further, the National Comprehensive Cancer Network® (NCCN®) makes no representations or warranties of any kind regarding their content, use, or application of the NCCN Guidelines and NCCN Guidelines Insights and disclaims any responsibility for their application or use in any way.

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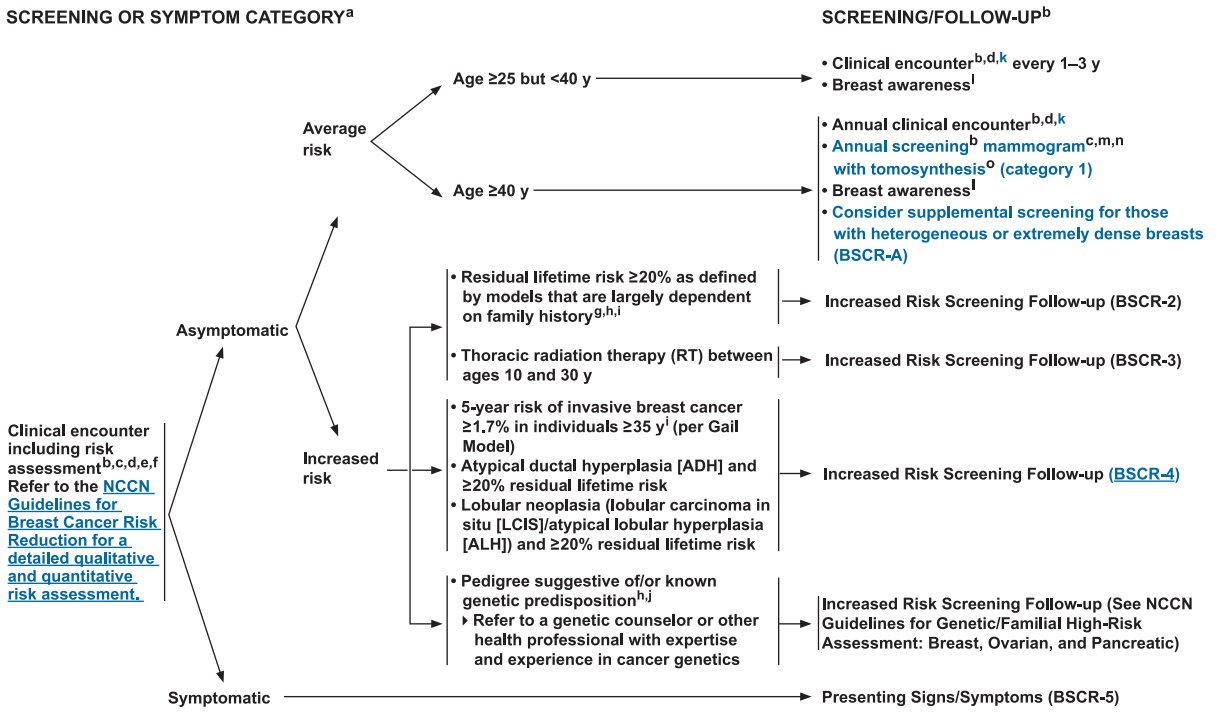


BSCR-1

Overview

The average lifetime risk of breast cancer for a female in the United States has been estimated at 12.3% (or 1 in 8 females).[1] For 2023, the American Cancer Society estimates that 300,590 cases of invasive breast cancer (299,540 in females and 2,800 in males) and 55,720 cases of female carcinoma in situ will be diagnosed in the United States.[2] About 43,700 breast cancer–related deaths are estimated for 2023.[2] Although breast cancer incidence rates increased by 0.5% each year from 2010 through 2019, mortality rates declined, falling an average of 1.3% each year from 2011 to 2020.[3] This decrease has been attributed to a combination of screening and treatment advances.[4]

Breast screening is performed in individuals without any signs or symptoms of breast cancer so that disease can be detected as early as possible. Earlier disease detection may decrease the overall treatment needed and reduce morbidity and mortality rates. Diagnostic breast imaging and evaluation differ from breast screening in that they are used to evaluate an existing problem (eg, palpable mass, discharge from the nipple, mammographic finding). NCCN screening recommendations are largely intended for cisgender females due to the preponderance of data in this population. For breast cancer screening of transgender individuals, the NCCN panel endorses the consensus-based guidelines developed by the American College of Radiology (ACR) Appropriateness Criteria.[5] Transgender individuals should consult with their primary care provider to determine when and/or whether screening would be appropriate.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer Screening and Diagnosis provide clinicians with a practical, consistent framework for screening and evaluating a spectrum of clinical breast presentations. These NCCN Guidelines Insights summarize the panel's decision-making and discussion surrounding the most recent updates to the guideline's screening recommendations. Recommendations on diagnosis and a complete list of the recent updates for 2023 are currently available in the complete version of these guidelines, available at NCCN.org.

Individuals are stratified into 2 basic categories of risk for the purpose of screening recommendations: average risk and increased risk of developing breast cancer. Risk assessment is outlined in the NCCN Guidelines for Breast Cancer Risk Reduction (available at NCCN.org). The increased risk category consists of 6 groups: (1) individuals who have a lifetime risk ≥20% as defined by models that are largely dependent on family history (eg, BRCAPRO,[6]

FOOTNOTES

[a] For individuals with a prior history of breast cancer, please refer to the NCCN Guidelines for Breast Cancer - Surveillance Section.
[b] Breast Screening Considerations (BSCR-A).
[c] Medicare and insurers allow the individual direct access to scheduling for screening mammography.
[d] At minimum, medical and family history should be reviewed and clinical encounter should encompass ongoing risk assessment, risk reduction counseling, and preferably a clinical breast examination (CBE) even in individuals who are asymptomatic when feasible.
[e] There is limited data on screening in individuals with increased risk for breast cancer assigned male at birth (AMAB).
[f] For pregnant and lactating individuals, see BSCR-B.
[g] Individuals with a residual lifetime risk of 15%–20% may be considered for supplemental screening on an individual basis, depending on risk factors.
[h] Risk models that are largely dependent on family history (eg, BRCAPRO, Tyrer-Cuzick, BOADICEA/CanRisk). See NCCN Guidelines for Breast Cancer Risk Reduction. There are significant limitations in interpretation of polygenic risk scores (PRS). PRS should not be used for clinical management at this time and use is recommended in the context of a clinical trial, ideally including diverse populations. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
[i] See Comparison of Predictive Models for Risk Assessment (NCCN Guidelines for Breast Cancer Risk Reduction).
[j] There is variation in recommendations for initiation of screening for different genetic syndromes. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
[k] Rationale for recommending clinical encounter is to maximize earliest detection of breast cancers and assure ongoing risk assessment, particularly in regions where mammographic screening may not be accessible. Randomized trials comparing incremental CBE versus mammographic screening have not been performed.
[l] Individuals should be familiar with their breasts and promptly report changes to their health care provider. See Symptomatic During Clinical Encounter, Presenting Signs and Symptoms (BSCR-5).
[m] Mammographic Evaluation (BSCR-18).
[n] Shared decision-making is encouraged based on individuals' values and preferences.
[o] Tomosynthesis can decrease call back rates and improve cancer detection compared with 2D mammography alone.

BSCR-1A

Tyrer-Cuzick,[7] BOADICEA/CanRisk[8]); (2) those who received prior thoracic radiation therapy (RT) between the ages of 10 and 30 years (eg, mantle irradiation); (3) those aged ≥35 years with a 5-year risk of invasive breast cancer ≥1.7% (per Gail model); (4) those who have a lifetime risk ≥20% based on history of atypical ductal hyperplasia (ADH); (5) those who have a lifetime risk ≥20% based on history of lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH); and (6) those with a known genetic predisposition or a pedigree suggestive of a genetic predisposition.

The components of a breast screening evaluation are dependent on age and other factors such as medical and family history, and can include breast awareness (ie, familiarity with one's own breasts); regular clinical encounters, which include breast cancer risk assessment and clinical breast examination (CBE); breast imaging with screening mammography; and, in selected cases, breast MRI with and without contrast or breast ultrasound.

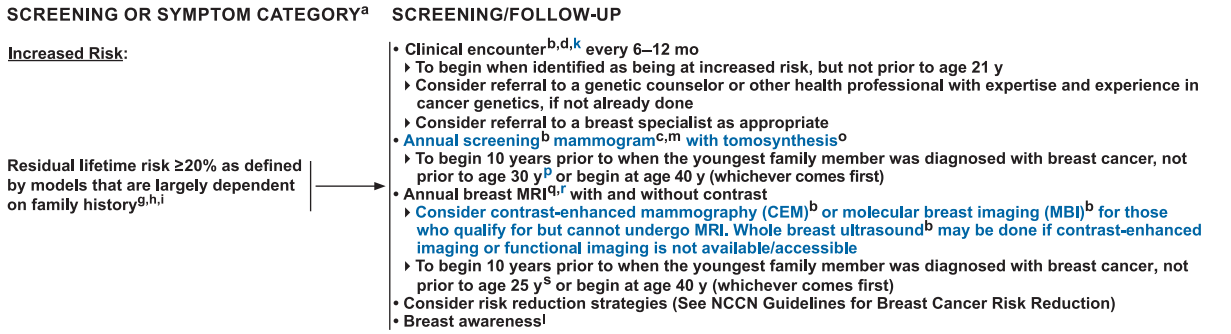
Clinical Encounters

The rationale for recommending clinical encounters is to maximize the earliest detection of breast cancers and ensure ongoing risk assessment. In the 2023 update, the panel notes that this is particularly true in regions where mammographic screening may not be easily accessible (see BSCR-1, BSCR-1A, and BSCR-2–4, pages 902–906). Although randomized trials comparing incremental CBE versus mammographic screening have not been performed, a study based in Mumbai, India, comparing CBE and cancer awareness information versus no screening revealed that the addition of CBE and cancer awareness information led to an earlier age at breast cancer diagnosis, a significant reduction in breast cancers diagnosed at stages III or IV, a nonsignificant reduction in mortality of 15% in the overall study population (ages 35–64 years), and a significant relative reduction in mortality of nearly 30% in individuals aged >50 years.[9]

Breast Imaging

Tomosynthesis

For the 2023 guidelines update, the panel modified the screening algorithm to make a stronger recommendation for all annual screening mammograms to be performed with tomosynthesis, regardless of risk category (see BSCR-1–4, pages 902–906). Previously, tomosynthesis was recommended, if available, in a separate bullet point from annual screening mammography.



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[m] Mammographic Evaluation (BSCR-18).
[o] Tomosynthesis can decrease call back rates and improve cancer detection compared with 2D mammography alone.
[p] Consider mammogram beginning at age 25 y on a case by case basis depending on family history.
[q] High-quality breast MRI requires a dedicated breast coil, access to biopsy under MRI guidance, experienced radiologists in breast MRI, and regional availability. MRI should be correlated with other breast imaging modalities.
[r] Many experts recommend alternating the mammogram and breast MRI with and without contrast every 6 months. While there is limited data to support this approach, the presumption is that this may lead to earlier identification of cancer.
[s] Except in rare circumstances of a family history of very early-onset breast cancers before age 30 years.

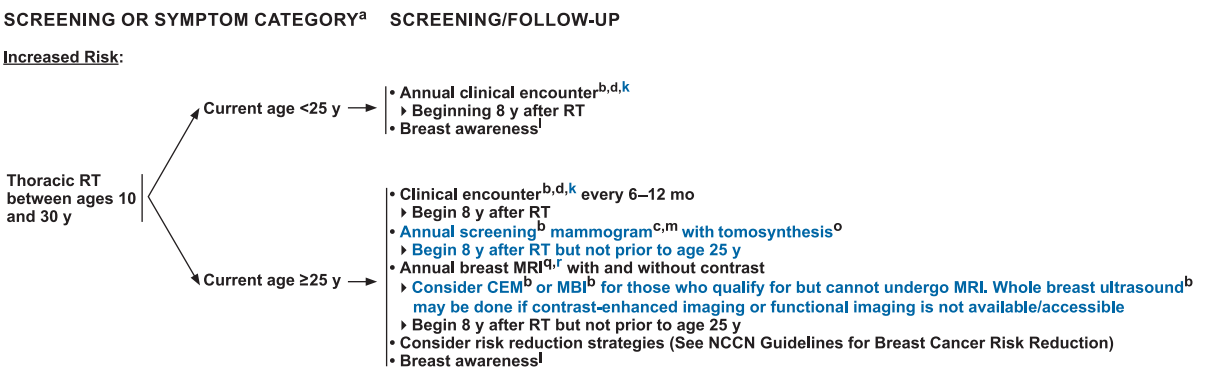
BSCR-2

Tomosynthesis has been shown to decrease false-positive callback rates and improve cancer detection compared with 2D mammography in several studies,[10–19] including for those with dense breasts.[20–24] Tomosynthesis allows acquisition of multiple low-dose x-ray images across a limited arc and a digital detector. These data are reconstructed using computer algorithms to generate thin sections displayed in a quasi-3D format. The combined use of 2D mammography and tomosynthesis results in double the radiation exposure compared with mammography alone. However, this increase in radiation dose falls below the dose limits of radiation set by the FDA for standard mammography. The radiation dose can be minimized by newer tomosynthesis techniques that create a synthetic 2D image from the tomosynthesis acquisition, which may obviate the need for a conventional digital image.[11,25,26] A meta-analysis comparing the use of synthetic 2D mammography versus standard 2D digital mammography with tomosynthesis revealed comparable diagnostic accuracy, with 85% versus 84% sensitivity and 93% versus 91% specificity, respectively.[27]

Supplemental Imaging

For many individuals considered at increased risk of breast cancer, annual breast MRIs with and without contrast are recommended in addition to annual screening mammograms with tomosynthesis. In the 2023 guideline update, the panel noted that many experts recommended alternating the mammogram and MRI every 6 months (see BSCR-2–4, pages 904–906). While the panel recognizes that there are limited data to support this approach, the presumption is that this may lead to earlier identification of interval cancers.[28] Mention was also made in the 2023 guideline update that abbreviated MRI has a higher cancer detection rate than mammogram with tomosynthesis and likely has similar sensitivity compared with full diagnostic protocol breast MRI.[29] Meta-analyses comparing abbreviated versus full diagnostic protocol MRI revealed similar sensitivity and specificity between the 2 modalities.[30,31]

For individuals who qualify for but cannot undergo MRI, the previous recommendation was to consider contrast-enhanced mammography (CEM) or whole breast ultrasound. In the 2023 guidelines update, although CEM is still recommended in this circumstance, the panel chose to replace whole breast ultrasound with molecular breast imaging (MBI) as another alternative to MRI. Whole breast ultrasound is now only recommended if contrast-enhanced imaging or functional imaging is not available/accessible (see BSCR-2–4, pages 904–906). There is



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[o] Tomosynthesis can decrease call back rates and improve cancer detection compared with 2D mammography alone.
[q] High-quality breast MRI requires a dedicated breast coil, access to biopsy under MRI guidance, experienced radiologists in breast MRI, and regional availability. MRI should be correlated with other breast imaging modalities.
[r] Many experts recommend alternating the mammogram and breast MRI with and without contrast every 6 months. While there is limited data to support this approach, the presumption is that this may lead to earlier identification of cancer.

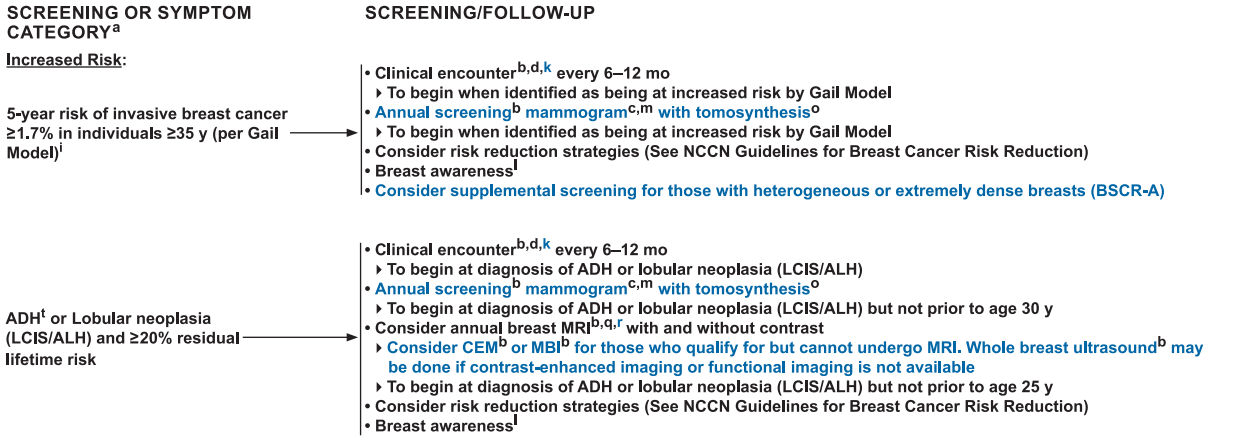
BSCR-3

emerging evidence that CEM and MBI may improve detection of early breast cancers among females with mammographically dense breasts.[32–35] CEM carries a risk of iodinated contrast reactions, although a systematic review revealed a pooled rate of adverse events of only 0.82%.[36] CEM also has a higher breast radiation exposure per examination than standard mammography, although the radiation dose remains below the dose limits set by the FDA for standard mammography.[32,36,37] Additionally, MBI has a whole-body effective radiation dose that is substantially higher than that of mammography.[32]

Breast Density

The presence of increased dense breast tissue decreases the sensitivity of mammography due to the obscuration or "masking" of cancers by overlying dense breast tissue. In addition, dense breast tissue as measured by mammography is increasingly recognized as an important risk factor for breast cancer.[38–41] Approximately half of all females of screening age have "dense" breast tissue referred to as "heterogeneously dense" or "extremely dense" by ACR Breast Imaging Reporting and Data System (BI-RADS) nomenclature.[42] Of note, the presence of dense tissue is not abnormal and can change over time. Although many individual states have passed legislation mandating patient notification of breast density,[43] not all states require insurance coverage for supplemental screening. Recently, the FDA issued a final rule, effective nationally by September 10, 2024, to update the Mammography Quality Standards Act by requiring a breast density assessment be reported to patients and health care providers (HCPs), with additional language notifying patients that in the setting of dense breast tissue, supplemental imaging studies beyond mammography may help detect cancer and recommending that individuals discuss their risk of breast cancer and review their personal preferences with their HCPs.[44]

Based on evolving requirements for reporting of breast density and increasing individual state insurance coverage for supplemental screening, in the 2023 guidelines update the panel added a statement to the algorithm recommending consideration of supplemental screening for individuals aged ≥40 years who have heterogeneously dense or extremely dense breast tissue and are otherwise considered at average risk of developing breast cancer (see BSCR-1, page 902). The risks and benefits of such screening should be discussed with individual patients.[45] Different supplemental imaging modalities may be considered based on risk and patient values/preference.[46] The ACR has published guidelines for supplemental screening based on breast density.[47]



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[r] Many experts recommend alternating the mammogram and breast MRI with and without contrast every 6 months. While there is limited data to support this approach, the presumption is that this may lead to earlier identification of cancer.
[t] Risk depends on age at diagnosis.

BSCR-4

Screening Recommendations for Specific Increased Risk Groups

Individuals With a Lifetime Risk ≥20% per Models Largely Dependent on Family History

A lifetime risk of breast cancer of ≥20% as assessed by models based largely on family history (eg, BRCAPRO,[6] Tyrer-Cuzick,[7] BOADICEA/CanRisk[8]) is a risk threshold used in the guidelines to identify an individual as a potential candidate for risk reduction strategies, as well as to direct screening strategies. A comparison of predictive risk models for risk assessment is outlined in the NCCN Guidelines for Breast Cancer Risk Reduction (available at NCCN.org).

Screening recommendations for individuals with a lifetime risk ≥20% as defined by models that are largely dependent on family history include breast awareness, consideration of risk reduction strategies in accordance with the NCCN Guidelines for Breast Cancer Risk Reduction, and a clinical encounter every 6 to 12 months beginning at the age identified as being at increased risk, but not prior to age 21 years. A referral to a genetic counselor or other health professional with expertise and experience in cancer genetics should be considered, if not already done. A referral to a breast specialist as appropriate should also be considered. Although the panel still recommends starting annual screening mammograms with tomosynthesis beginning 10 years prior to when the youngest family member was diagnosed with breast cancer, but not prior to age 30 years, or beginning at age 40 years (whichever comes first), in the 2023 guideline update, the panel added a footnote that beginning annual screening mammograms with tomosynthesis at age 25 years can be considered on a case-by-case basis, depending on the family history (see BSCR-2, page 904). Multiple panel members recognize that they treat an increasing number of individuals with breast cancer between the ages of 25 and 30 years and that they prefer not to delay screening mammography until age 30 years for individuals with family members diagnosed with breast cancer within this earlier age range. Although there is the option to begin annual breast MRI with and without contrast at age 25 years (to begin 10 years prior to when the youngest family member was diagnosed with breast cancer, but not prior to age 25 years, or beginning at age 40 years [whichever comes first]), it was noted that MRI may not be available in smaller or more rural community practices.

Individuals Who Received Thoracic RT Between Ages 10 and 30 Years

Results from several studies have demonstrated that females who received thoracic RT in their second or

third decade of life have a substantially increased risk of developing breast cancer by age 40 years.[48–53] For example, in the Late Effects Study Group trial, the overall risk of breast cancer associated with prior thoracic RT at a young age was found to be 56.7-fold (55.5-fold for female patients) greater than the risk of breast cancer in the general population.[49,52] The relative risk of female breast cancer according to follow-up interval was 0 at 5–9 years; 71.3 at 10–14 years; 90.8 at 15–19 years; 50.9 at 20–24 years; 41.2 at 25–29 years; and 24.5 at >29 years.[52] Results from a case-control study of females treated with thoracic RT at a young age for Hodgkin lymphoma indicated that the estimated cumulative absolute risk of breast cancer at age 55 years was 29.0% (95% CI, 20.2%–40.1%) for a female treated at age 25 years with at least 40 Gy of radiation and no alkylating agents.[54] Unfortunately, findings from a survey of breast screening practices in this population of patients suggest that a sizable segment of this group is not undergoing regular mammographic screening.[55]

Screening recommendations for individuals that received thoracic RT between ages 10 and 30 years and are currently aged <25 years include an annual clinical encounter beginning 8 years after RT and breast awareness. For those currently aged ≥25 years, breast awareness is recommended, and clinical encounters are recommended every 6 to 12 months beginning 8 years after RT. In addition, individuals in this risk group should be counseled on risk-reduction strategies in accordance with the NCCN Guidelines for Breast Cancer Risk Reduction (available at NCCN.org). Although the panel still recommends starting annual screening mammograms with tomosynthesis 8 years after RT for individuals who have undergone thoracic RT between the ages of 10 and 30 years, the recommendation was previously to delay this until age 30 years, whereas in the 2023 guideline update, the panel updated its recommendation to delay only until age 25 years (see BSCR-3, page 905). As previously mentioned, multiple panel members acknowledged the increasing number of individuals being diagnosed with breast cancer between the ages of 25 and 30 years, and that although annual MRI with and without contrast is recommended 8 years after RT but not prior to age 25 years, MRI may not be available in smaller or more rural community practices. Also, in a prospective study comparing MRI with mammography in females who had received chest RT for Hodgkin lymphoma, MRI missed 6 breast malignancies that were detected by mammogram, all with suspicious calcifications.[56] These points all impacted the decision to allow for mammographic screening beginning at this earlier age range, along with MRI. Although there is a concern that the cumulative radiation exposure from mammography in a young individual may itself pose a risk for cancer, it is felt that the additional radiation in this population is negligible compared with overall radiation exposure.

Individuals Aged ≥35 Years With 5-Year Risk of Invasive Breast Cancer ≥1.7% per Modified Gail Model

Although most screening guidelines are based on lifetime risk of breast cancer, the NCCN Guidelines do include the increased risk category of 5-year risk of invasive breast cancer ≥1.7% per the modified Gail model in individuals aged ≥35 years.[57–61] The modified Gail model assesses the risk of invasive breast cancer as a function of age, menarche, age at first live birth or nulliparity, number of first-degree relatives with breast cancer, number of previous benign breast biopsies, atypical hyperplasia in a previous breast biopsy, and race. The model calculates 5-year and lifetime projected probabilities of developing invasive breast cancer and can be used to identify individuals at increased risk.

Screening recommendations for individuals aged ≥35 years with 5-year risk of invasive breast cancer ≥1.7% per the modified Gail model include breast awareness, a clinical encounter every 6 to 12 months, and annual mammography with tomosynthesis, to begin at the age identified as being at increased risk by the Gail model. In addition, according to the panel, individuals in this group should be counseled on risk-reduction strategies in accordance with the NCCN Guidelines for Breast Cancer Risk Reduction (available at NCCN.org).

Mirroring the recommendation for individuals in the average risk category aged >40 years, in the 2023 guideline update, the panel added the recommendation to consider supplemental screening for individuals in this risk category who have heterogeneously dense or extremely dense breast tissue as well, as this is the only increased risk category where annual MRI is not explicitly recommended as a supplement to annual screening mammography with tomosynthesis (see BSCR-4, page 906).

Individuals With ADH or Lobular Neoplasia and ≥20% Residual Lifetime Risk

Screening recommendations for individuals with ADH or lobular neoplasia (LCIS/ALH) and ≥20% residual lifetime risk of breast cancer include a clinical encounter every 6 to 12 months to begin at diagnosis of ADH or lobular neoplasia, breast awareness, counseling on risk-reduction strategies in accordance with the NCCN Guidelines for Breast Cancer Risk Reduction (available at NCCN.org), and annual screening mammogram with tomosynthesis to begin at diagnosis of ADH or lobular neoplasia but not prior to age 30 years. It is also recommended to consider annual breast MRI with and without contrast. Consideration was made for changing this recommendation from annual breast MRI to a broader recommendation for contrast or physiologic imaging (CEM, MRI, or MBI). A study examining cancer detection rates with mammography alone versus mammography in addition to MRI in a large

cohort of females with LCIS was discussed, in which MRI did not lead to increased cancer detection rates.[62] A more recent, similar study was also discussed, which also revealed a lack of improvement in cancer detection rates with screening MRI in females with LCIS as well as ADH and ALH and also revealed a significantly higher biopsy rate with the use of mammogram and MRI combined.[63] Despite the discussion surrounding these 2 studies, the panel ultimately decided to keep its recommendation to consider annual breast MRI with and without contrast given concern for missing an invasive lobular carcinoma with mammography alone and given that there are more published studies in this population investigating MRI compared with CEM or MBI (see BSCR-4, page 906). Although there are emerging data for CEM in this population,[34,64–67] most studies have included a mixed population of increased risk groups rather than ADH or lobular neoplasia specifically. Like other increased risk groups, CEM or MBI can be considered for those who qualify for but cannot undergo MRI.

Summary

The goal of breast screening is to detect breast cancer as early as possible, prior to the onset of signs or symptoms of disease, to allow for earlier, less aggressive treatments, thus reducing the mortality and morbidity associated with the disease. These NCCN Guidelines Insights highlight important recent updates to screening recommendations in the NCCN Guidelines for Breast Cancer Screening and Diagnosis, including but not limited to an increased emphasis on tomosynthesis and updated supplemental imaging recommendations.

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