Breast Density Legislation
Implications for Patients and Primary Care Providers

BY DEBORAH J. RHODES, M.D., AND AMY LYNN CONNERS, M.D.

Minnesota recently became the 16th state to require facilities that perform mammograms to notify patients if they are found to have dense or extremely dense breasts, as this may make it more difficult to detect a cancer or put them at increased risk for cancer. This article outlines the new law and describes the classification system for breast density, the implications for breast density on screening mammography, and the relationship between breast density and cancer. It also provides guidance for patients who have dense breast tissue regarding supplementary screening.

On May 21, Minnesota became the 16th state to enact a breast density notification law. The new law, which was included in a broader omnibus health care bill, states that mammography patients must be notified in writing if they are found to have dense or extremely dense breast tissue, as this may make it more difficult to detect and place them at increased risk for breast cancer.

This law has implications for women and for physicians and other health care providers. Although radiologists have for years routinely reported breast density information in the mammography report, such information has not been included in the federally mandated letter sent to patients following a mammogram. Starting August 1, facilities will be required to include this information in the letter. The purpose of this article is to assist those who will be discussing the implications of breast density with women and participating in shared decision-making with them regarding supplemental breast cancer screening.

What is Breast Density?
The breast is composed of fat and fibroglandular tissue, which includes both epithelial tissue (ducts and lobules) and connective tissue. There is wide variability among women in the ratio of fat to fibroglandular tissue in their breasts. Breast density is a measure of breast tissue composition based on mammographic appearance. Dense breasts have proportionately more fibroglandular tissue visible on a mammogram than nondense breasts. Fat is radiologically lucent and appears dark on a mammogram, whereas fibroglanular tissue is radiologically dense and appears light on a mammogram.

Classification of Breast Density
Breast tissue ranges from predominantly fatty to extremely dense. There are various methods of classifying breast density, but the most common one is the American College of Radiology’s Breast Imaging Reporting and Data System (BI-RADS), which classifies breast density into four categories (Table 1). Dense breasts are described as either heterogeneously or extremely dense. Radiologists reading mammograms estimate the amount of fibroglandular tissue within the breast and must include one of four descriptors in their mammography report (Figure 1). There is no correlation between density and breast size, texture or fibrocystic changes.

In editions of the BI-RADS Atlas prior to 2013, percentages (increments of 25%) were associated with the categories. The percentages were eliminated in the 2013 edition to emphasize the subjective nature of estimating breast density and the masking effect of dense fibroglandular tissue on the mammographic depiction of noncalcified cancers.

There is considerable variation in estimating breast density. Quantitative methods exist but are not used in routine clinical practice.

According to data from the Breast Cancer Surveillance Consortium, a network of seven mammography registries in the United States, there has been very little change in the distribution of mammograms over the four density categories since 1996. In 2009, 10% of mammograms were classified as fatty, 43% were classified as having scattered areas of fibroglandular density, 39% were heterogeneously dense and 8% were extremely dense. Therefore, approximately 47% of screening mammograms in the United States are classified as dense.

Implications of Breast Density on Mammography Screening
Breast density increases the likelihood of both false-negative and false-positive mammography findings.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Breast Composition Categories*</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>The breasts are almost entirely fatty.</td>
</tr>
<tr>
<td>b)</td>
<td>There are scattered areas of fibroglandular density.</td>
</tr>
<tr>
<td>c)</td>
<td>The breasts are heterogeneously dense, which may obscure small masses.</td>
</tr>
<tr>
<td>d)</td>
<td>The breasts are extremely dense, which lowers the sensitivity of mammography.</td>
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</tbody>
</table>

*Defined by the American College of Radiology’s Breast Imaging Reporting and Data System (BI-RADS) 2103 Atlas
Breast Density and Breast Cancer Risk

The association between mammographic breast density (MBD) and breast cancer risk has been investigated in more than 60 studies. These studies differ in their classification of breast density and in the cut-off points delineating women with dense breasts from controls. Nevertheless, the association between breast density and breast cancer risk is strong and independent of the influence of other risk factors.

A meta-analysis of 42 studies found that the relative risk of breast cancer was 1.79 (95% CI, 1.48 to 2.16) in women with 5% to 24% density; 2.11 (1.70 to 2.63) for women with 25% to 49% density; 2.92 (2.49 to 3.42) for women with 50% to 74% density; and 4.64 (3.64 to 5.91) for women with >75% density.

Boyd et al. reported an odds ratio of 4.7 for women with >75% mammographic density relative to those with <10% density (95% CI, 3.0, 7.4) after adjusting for age, body mass index (BMI) score, age at menarche, parity, number of live births, age at first birth, menopausal status, age at menopause, hormone therapy use and breast cancer in first-degree relatives. Only age and BRCA mutation status are associated with larger relative risks of breast cancer than MBD when comparing the highest to the lowest categories of density. The increased cancer risk associated with breast density has been shown to persist at least eight years after measurement.

Breast cancer risk prediction models that incorporate breast density have been developed, but they improve the discriminatory power of existing models only incrementally and are not used routinely in clinical practice.

False Negatives

The sensitivity of mammography is lower in women with dense breasts than in those with fatty breasts. In an evaluation of 329,495 mammograms, the sensitivity of mammography in women with extremely dense breasts was 63% compared with 87% in women with fatty breasts. Other studies have demonstrated mammography sensitivities as low as 30% in women with dense breasts. The decreased sensitivity is the result of the masking effect of density. Because the X-ray attenuation characteristics of tumors can be indistinguishable from the surrounding density, tumors that occur in areas of dense tissue can be occult or difficult to discern on mammography (Figures 2a, 2b).

The masking effect also explains the higher rate of interval cancers seen in women with dense breasts. Boyd et al. found the odds ratio of a cancer detected less than 12 months after a negative screening examination was 17.8 (95% CI, 4.8 to 65.9) in women with extensive breast density as compared with those (leading to additional mammogram, ultrasound or MRI imaging, and sometimes biopsy) after 10 years of annual screening exceeded 60% for women ages 40 to 49 years with heterogeneously or extremely dense breasts vs. 5.5% for women in that same age group with fatty breasts. Studies have reported a three-fold increase in the risk of a false-positive mammogram finding in women with dense breasts as compared with those with fatty breasts.

False Positives

Breast density is associated with reduced specificity of mammography. Kerlikowske et al. found that the cumulative probability of a false-positive mammography result
In addition to overall risk, high breast density is associated with larger tumor size,\(^9,20\) high histologic grade, lymphovascular invasion, advanced stage and positive lymph nodes.\(^{20-22}\) MBD also may be associated with increased local recurrence and risk of a second primary breast cancer.\(^{23,24}\) Two large retrospective studies found no association between high breast density and breast cancer-specific survival.\(^{25}\)

**TABLE 2**

**Impact of Breast Density**

<table>
<thead>
<tr>
<th>Impact</th>
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</thead>
<tbody>
<tr>
<td>Mammography sensitivity decreases</td>
</tr>
<tr>
<td>Mammography specificity decreases</td>
</tr>
<tr>
<td>Interval cancer risk increases</td>
</tr>
<tr>
<td>Breast cancer risk increases</td>
</tr>
<tr>
<td>Risk of larger tumor size at diagnosis</td>
</tr>
<tr>
<td>Risk of positive lymph nodes at diagnosis</td>
</tr>
<tr>
<td>Risk of advanced-stage disease* increases</td>
</tr>
<tr>
<td>No apparent effect on survival</td>
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</tbody>
</table>

*Risk increases further in women with dense breasts who use postmenopausal hormone therapy.

**Association between Breast Density and Other Breast Cancer Risk Factors**

Mammographic breast density is correlated with multiple breast cancer risk factors. The strongest associations are seen with age and BMI.\(^{18,26,27}\) However, even after adjusting for these and other breast cancer risk factors, there remains a robust and independent association between MBD and breast cancer risk.

At a population level, age is inversely related to MBD, but age is not a sufficient surrogate for MBD because of considerable individual variation. Twin studies have shown that inherited factors explain 63% of the variation in density in the population at any given age.\(^{28}\) Nevertheless, the proportion of women with MBD decreases with each subsequent decade of life after initial screening (74% for women ages 40 to 49; 57% for women ages 50 to 59; 45% for women ages 60 to 69; and 36% for women ages 70 to 79).\(^{29}\)

MBD is inversely associated with BMI as well as weight gain after age 18.\(^{30}\)

MBD is also influenced by reproductive and hormonal factors. MBD is inversely associated with parity.\(^{10,31}\) Use of hormone therapy for at least one year has been shown to increase MBD in approximately 16% to 20% of women, with average increases of 3% to 5% for those using estrogen and progestin and 1.6% for those using estrogen alone.\(^{32-35}\) MBD has been shown to decline with cessation of hormone therapy.\(^{36}\) Among women with extremely dense breasts, use of combination hormone therapy compounded their breast cancer risk: Among women 55 to 59 years of age with extremely dense breasts, the five-year risk of breast cancer was 4.2% for those who use estrogen plus progestin (95% CI, 3.7% to 4.6%), 3.0% among those who use estrogen only (95% CI, 2.6% to 3.5%) and 2.4% for those who do not use hormone therapy (95% CI, 2.0% to 2.8%).\(^{32}\) Therefore, postmenopausal women with very high MBD should consider the added risk of breast cancer when making decisions about hormone therapy and especially combination hormone therapy.

**Discussing Breast Density with Patients**

There are two issues physicians need to discuss with patients who have dense breasts. One is the impact of breast density on breast cancer detection and risk (Table 2). Women need to understand the limitations of mammography so they report breast changes or concerns even after having a “negative” mammogram. Understanding the impact of MBD on breast cancer risk may also assist them in making health decisions, such as whether to use hormone therapy.

The second issue to discuss is supplemental screening. In discussing this, phy-
Talking Points for Physicians

- Having dense breast tissue is common, but it increases the chance that a cancer won’t be visible on a mammogram; a patient with dense breasts may have a higher risk of developing breast cancer than one who doesn’t have dense breasts.
- If a woman notices a change in her breasts, even if her mammogram is normal, she should be evaluated promptly. Focused mammogram and ultrasound can be used to look more closely at an area of concern.
- Supplemental screening tests don’t replace the mammogram, but they can be used to help the radiologist better see through dense tissue.
- A supplemental screening test may find a cancer that isn’t visible on a mammogram. It may also show findings that are not cancer and may lead to biopsies and/or additional breast imaging studies. Insurance may or may not pay for the supplemental screening tests.
- There are some types of breast cancer for which early detection may not improve survival. There are other types that may not be life-threatening; finding these means a patient will receive treatment that won’t prolong her life. At this time, we are unable to identify which cancers may not require treatment.
- We do not yet know whether supplemental screening can save lives. More research is needed to compare the available tests and to determine if they benefit women with dense breasts.

Physicians should make sure patients understand these points:

- The goal of supplemental screening of the dense breast is to detect tumors obscured by MBD.
- The impact of supplemental screening on breast cancer mortality is unknown. No studies have examined the impact of supplemental screening of women with dense breasts on breast cancer mortality. The correlation between breast cancer survival and tumor size and lymph node status has fueled the assumption that earlier detection of breast tumors through additional screening will improve the chance of survival, but advances in the understanding of tumor biology have identified associations between molecular signatures and survival that may be less dependent on time of detection. Currently there is no consensus in the radiology community about whether supplemental screening will depend on the patient’s perception of the risks of overdiagnosis and false-positive findings versus the potential benefit of detecting cancers that may be masked by MBD.

Supplemental Screening Options

Currently, there are three main options (with several others being studied and in development) for supplemental screening of women who do not qualify for screening MRI. No trial has directly compared these modalities, and most breast imaging facilities do not offer all of them.

Digital breast tomosynthesis. With digital breast tomosynthesis, a series of thin-resolution X-ray images are aggregated to generate a 3D image of the breast, reducing artifact caused by overlapping dense tissue seen on traditional 2D images. Digital breast tomosynthesis is the only supplemental screening modality that has been shown to reduce rather than increase the number of false-positive findings associated with mammography. However, the increased diagnostic yield is lower than that reported for other supplemental screening modalities. With tomosynthesis, there is a small increase in radiation exposure, although techniques under development may allow for imaging at the same dose as traditional mammography.

Screening ultrasound. Unlike targeted ultrasound performed for diagnostic purposes, screening ultrasound scans the entire breast using either a hand-held or automated transducer. Screening ultrasound is associated with the highest risk of false-positive findings among the supplemental modalities. One advantage is the absence of radiation exposure.

Molecular breast imaging. Molecular breast imaging (MBI) provides a functional breast image based on preferential uptake of 99mTc-sestamibi in tumors relative to normal tissue, independent of breast density. Unlike imaging done with older-generation scintillating gamma cameras, MBI directly converts gamma ray energy to electronic signal through solid-

modality offers the best risk-to-benefit ratio. Ultimately, the decision to pursue supplemental screening will depend on the magnitude of overdiagnosis and the potential benefit of detecting cancers that may be masked by MBD.
state cadmium zinc telluride detectors. MBI has the highest reported supplemental cancer detection rate of the three modalities in blinded clinical trials, although no direct comparison has been performed. MBI requires an injection and is associated with more radiation exposure than mammography, although it is still within an acceptable range for a screening modality. MBI has been extensively studied at Mayo Clinic Rochester and is the recommended modality for supplemental screening at this site; but access to MBI is limited in other parts of Minnesota. 9,46-47

Physicians and patients should consider the available evidence regarding the relative diagnostic performance of supplemental screening options, including diagnostic yield, false-positive rate and biopsy rate (Table 3). Important additional considerations include patient preferences and comfort, radiation exposure, availability of tests, radiologist expertise, insurance coverage and cost. It is particularly important to caution patients that supplemental screening may not be covered by their insurance.

It should be noted that MRI has a high sensitivity for the detection of cancer in dense breast tissue. 45 However, screening MRI is not recommended for women with MDB unless they have additional risk factors. 46 Annual screening MRI is indicated, regardless of MDB, for women with any of the following risk factors:
- Having a lifetime risk of breast cancer of 20% to 25% or greater, according to risk assessment tools based on family history
- Having a BRCA1 or BRCA2 gene mutation
- Having a first-degree relative with a BRCA1 or BRCA2 gene mutation, but not having had genetic testing themselves
- Having received radiation therapy to the chest between the ages of 10 and 30 years
- Having Li-Fraumeni syndrome, Cowden syndrome or Bannayan-Riley-Ruvalcaba syndrome, or a first-degree relative with one of these syndromes.

When eligibility for screening MRI is in question, referral to a breast specialty clinic or medical geneticist should be considered.

**Conclusion**

Because Minnesota law now requires mammography facilities to notify women if they have dense breasts, physicians should be prepared to discuss the implications of breast density on breast cancer detection and risk and to participate in shared decision-making with patients who may require supplemental screening.

Along with talking to patients about mammography and breast cancer, they should stress the fact that supplemental screening should be done in addition to, not instead of, annual mammography. And they should encourage premenopausal women to schedule their screening mammogram during the first and second weeks of the menstrual cycle instead of during the third and fourth weeks, as breast tissue is less radiographically dense during this time. 48 They also should encourage women to become familiar with what is normal for their breasts and report any changes, and to make healthy lifestyle choices in order to reduce their risk for breast cancer. These include maintaining a healthy weight, 30,31 exercising regularly, 32 limiting alcohol intake 33 and limiting use of postmenopausal hormone use. 34-36

Minnesota’s new law offers an opportunity to engage women in important discussions about their health. MM

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**REFERENCES**


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**TABLE 3**

**Comparison of Supplemental Screening Modalities**

<table>
<thead>
<tr>
<th>MODALITY</th>
<th>SUPPLEMENTAL CANCER DETECTION RATE PER 1,000 SCREENED</th>
<th>RECALL RATE RELATIVE TO MAMMOGRAPHY ALONE</th>
<th>BIOPSY RATE</th>
<th>OTHER CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomosynthesis</td>
<td>1.9 to 2.852</td>
<td>Decreased by 3.2% to 17.2%3</td>
<td>Not reported</td>
<td>Effective radiation dose: 1.2 mSv</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>3.5 to 4.4147</td>
<td>Increased by 15.1%5</td>
<td>7.8%3</td>
<td>No radiation exposure</td>
</tr>
<tr>
<td>Molecular Breast Imaging</td>
<td>8.814</td>
<td>Increased by 6.6%6</td>
<td>2.9%6</td>
<td>Effective radiation dose: 2.0 mSv</td>
</tr>
</tbody>
</table>


