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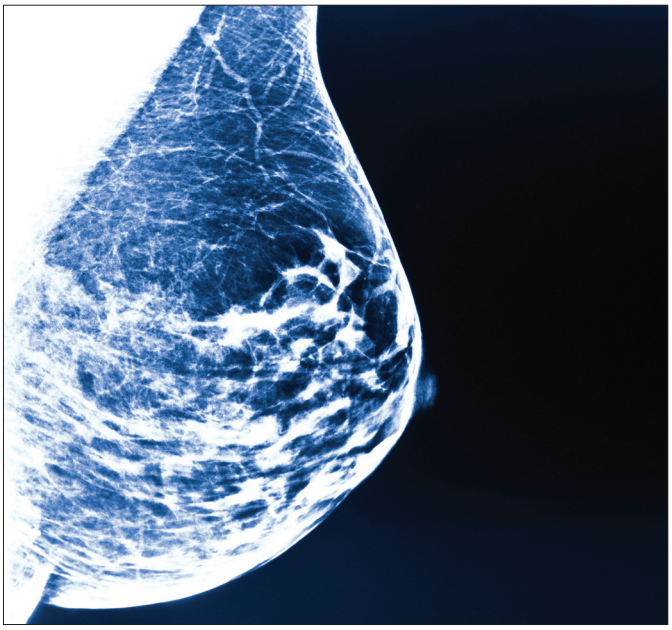

Breast Density

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Awareness of breast density by patients and providers has grown dramatically in the past several years – largely due to legislation passed by many states that requires women to be notified of their breast density. Despite increasing awareness, education on breast density seems to be lagging. Understanding how breast density matters for women's health, and what the clinical implications are, is critical as legislation expands.

Epidemiology and Measurement of Breast Density

Breast density refers to the appearance of breast tissue by mammography that indicates how much of the tissue is fat rather than glandular or connective tissue (fibroglandular). Having more fibroglandular tissue relative to fatty tissue leads to higher breast density, which is now well established as being associated with increased risk of breast cancer. Breast density on mammography is usually determined by radiologists' visual assessment of the images, and is clinically categorized into levels 1-4 (lowest-highest) according to the Breast Imaging Reporting and Data Systems (BI-RADS) for density. The BIRADS density score corresponds to the percent of dense tissue seen on the mammogram: almost entirely fatty (< 25% fibroglandular tissue, BIRADS 1, lowest density), scattered fibroglandular tissues (25–50% fibroglandular tissue, BIRADS 2), heterogeneously dense (51–75% fibroglandular tissue, BIRADS 3), and extremely dense (> 75% fibroglandular tissue, BIRADS 4, most dense) [D'Orsi 2003]. Efforts are underway to implement more objective, quantitative density measures, including volumetric as digital breast tomosynthesis use expands, but currently density measurement is largely subjective based on radiologists' visual assessment. Every mammographic report will have a BIRADS density category for that woman's mammogram. In the U.S., about 10% of women have almost entirely fatty breasts, about 10% have extremely dense breasts, and 80% are in the two middle categories. (ACR) Thus, about 25 million women age 40-74 may have dense breasts (BIRADS 3 or 4), which places them at some increased risk of developing breast cancer. (Sprague, ACR) Dense breasts are more common among younger women, especially those who are premenopausal, and less common among women with high body mass index (BMI).

Density and Breast Cancer Risk

The concern over breast density is due to its associated increased risk of breast cancer incidence. Overall, women with extremely dense breasts have a greater than fourfold increased risk of a breast cancer diagnosis compared to women with fatty breasts. (Boyd, Yaghjyan) However, comparing risk for the highest and lowest density categories informs the smallest groups of women: the approximately 10% with extremely dense breasts and the approximately 10% with almost entirely fatty breasts. (Price, ACR) When breast cancer risk is compared to average breast density, women with somewhat denser breasts (40% of women) is 1.2 times greater than average, and for the 10% with extremely dense breasts, it is about 2.1 times greater. (Sickles) While denser breasts increase risk for both pre- and postmenopausal women (density often declines after menopause), body mass index (BMI) modifies the effect of density on breast cancer risk. This effect is opposite for pre- and postmenopausal women; it is associated with a decreased breast cancer risk for women prior to menopause, but an increased risk after. (Pettersson)

Importantly, breast density affects risk of a breast cancer diagnosis through two main mechanisms: 1) masking of lesions on mammograms, and 2) biological action. The biological basis of increased breast cancer risk associated with dense breasts continues to be studied. Currently, the molecular and cellular basis of risk from dense breast tissue is not well understood, but studies – including several using data from women in the New Hampshire Mammography Network – have shown that breast cancer arising in areas of dense tissue are associated with poorer prognosis tumor characteristics, such as large size, invasiveness, and advanced stage. (Aiello, Yanghjiyan, Kerlikowske) Dense breasts also appear to be associated with increased local recurrence and risk of a second primary breast cancer. (Cil, Buist) Despite the association of dense breasts with poorer prognostic features, and risk of a second breast cancer event, two key studies demonstrated that there was no greater risk of death from breast cancer with denser breasts. (Maskarinec, Gierach)

The second mechanism of increased risk of breast cancer with dense breasts is the masking effect. Dense breast tissue appears white on mammography, and thus can obscure, or "mask" breast lesions that may be present, particularly small ones. The sensitivity of mammography with fatty (low density) breasts is 88%, while for women with the densest breasts, it is only 62%. (Carney, Kolb) It is largely because of this lower mammographic sensitivity that use of supplemental screening modalities has been implemented in some situations. The distinction between these two mechanisms by which density contributes to risk of breast cancer – biological and radiographic masking – is critical given the widely disparate ways they can be addressed. For the biological aspect of breast density, women with dense breasts can reduce risk by limiting or discontinuing use of hormone replacement, can modify other risk factors, such as BMI, and in some cases, may consider chemoprevention, such as

tamoxifen. (Wang) For the masking problem found with dense breasts, supplemental imaging may be warranted.

Supplemental Imaging for Women with Dense Breasts

Supplemental imaging for women with dense breasts typically refers to ultrasound, magnetic resonance imaging (MRI), or digital breast tomosynthesis (DBT), sometimes referred to as 3-D mammography. Studies have shown that ultrasound and MRI can detect cancers not able to be seen by mammography in dense breasts. But both ultrasound and MRI also detect more findings that are not cancer and may lead to further testing and biopsies, so research is underway to identify the most effective use of supplemental imaging. Much uncertainty currently exists for use of supplemental imaging for women with dense breasts, largely due to lack of evidence-based guidelines for which modality(ies) should be used in specific clinical contexts and whether all women with dense breasts should undergo supplemental screening, or only those with additional risk factors. (Ho) While evidence accrues, the dominant recommendation is to consider supplemental imaging in conjunction with other breast cancer risk factors, the degree of density, and women's preferences. Some states that have breast density notification legislation are also mandating or recommending supplemental imaging.

Breast Density Legislation

Legislation requiring that women be notified of their breast density following mammography first began in 2009 in Connecticut, based in part on the efforts of Nancy Capello, whose advanced breast cancer was diagnosed without her awareness that that prior mammography had shown her to have dense breast tissue. Since 2009, breast density legislation has been passed in 24 states, and 10 others have legislation in process. American Society of Clinical Oncology. Some states are also mandating that insurance cover supplemental imaging for women with dense breasts (CT web, Modern Health), but such policy is not in place in most states. The intent of such legislation is to give women information on their breast density so they can discuss their overall risk with their providers and decide if further imaging or testing is warranted.

Notification of breast density is often done by letter, and may or may not provide adequate understanding about what a woman's density category means for her. While the movement for breast density notification legislation has been driven by grassroots organizations and popular support, medical organizations have been more cautious. (Slanetz) The New Hampshire Breast Cancer Coalition Board of Directors favors education over legislation for breast density, and there is not currently legislation in New Hampshire underway, although it has been considered. While it is important for women and providers to know breast density and to factor it in to a woman's breast cancer risk profile and clinical decision making, some imaging experts and organizations feel that it is premature to legislate these matters while density determination is still subjective and effective use of supplemental imaging is not yet clear. Nevertheless, breast density legislation provides an opportunity for women to become more informed and aware of their breast health, and to strengthen patient-provider relationships through discussion of risks, benefits, and preferences.

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