

NEW NOTIFICATION REQUIREMENT

Breast Density

Michigan is the 21st state to adopt legislation mandating that women be informed if they have “dense breast tissue” on screening mammography. Already breast imaging centers are required by law to notify patients of their mammography results; this new specific finding will be added to that notification. The verbiage in the notification is mandated by law and reads as follows:

“Your mammogram shows that your breast tissue is dense. Dense breast tissue is very common and is not abnormal. However, dense breast tissue can make it harder to find cancer through a mammogram. Also, dense breast tissue may increase your risk for breast cancer. This information about the result of your mammogram is given to you to raise your awareness. Use this information to discuss with your health care provider whether other supplemental tests in addition to your mammogram may be appropriate for you, based on your individual risk. A report of your results was sent to your ordering physician. If you are self-referred, a report of your results was sent to you in addition to this summary.”

Breasts are composed of fat and fibroglandular tissue. Breasts are considered radiographically dense if they contain a majority of fibroglandular tissue. Fibroglandular tissue and breast masses appear similar on conventional (2 dimensional or 2D) mammography. This can cause “masking” of a mass on mammography. As a result, standard mammography can be less accurate in women with dense breasts, prompting the notification to alert women of this variant. Breast density should

be reported with the following nomenclature on mammogram reports:

WHAT IS BREAST DENSITY?

- A.** The breasts are almost entirely fatty.
- B.** There are scattered areas of fibroglandular density.
- C.** The breasts are heterogeneously dense, which may obscure small masses.
- D.** The breasts are extremely dense, which lowers the sensitivity of mammography.

HOW COMMON ARE DENSE BREASTS?

Approximately 50% of women undergoing screening mammography are classified as having either “heterogeneously dense” or “extremely dense” breasts. For all of these women, the patient letter will inform them that they have “dense breast tissue.”

Only 10% of all women have “extremely dense” breast tissue, which is associated with a relative risk of breast cancer of approximately 2 compared with average breast density. 40% of women have “heterogeneously dense” breast tissue, which is associated with a relative risk of approximately 1.2. Therefore, breast density is not a major cancer risk factor.

HOW HIGH IS THE CANCER RISK ASSOCIATED WITH BREAST DENSITY?

Consider the risk that an average woman will be diagnosed with breast cancer during the next 10 years of her life:

Age 30: 0.44% (1 in 227)

Age 40: 1.47% (1 in 68)

Age 50: 2.38% (1 in 42)

Age 60: 3.56% (1 in 28)

Age 70: 3.82 % (1 in 26)

The medical literature on the impact of density on this cancer risk is often misleading because most studies describe the risk by comparing the 10% of women in the highest density category (extremely dense) with the 10% of women in the lowest density category (almost entirely fatty). This is not meaningful to the other 80% of women, nor should risk comparisons be related to such a small subset of the patient population. When risk is expressed relative to average breast density (between scattered areas of fibroglandular density and heterogeneously dense), the risk for the 40% of women with heterogeneously dense breasts is only about 1.2 times greater and the risk for the 10% of women with extremely dense breasts is only about 2 times greater. (so instead of 1 in 68 at age 40, the risk is 1 in 32). Therefore, breast density is not a major cancer risk factor.

RISK ASSESSMENT

Determination of a patient's overall breast cancer risk is important, as density alone is not a reason to further imaging. Several tools can be used to stratify women into risk groups. The Gail Risk Score is a statistical model developed by the NCI to help determine who may be at elevated risk for breast cancer, it allows a starting point for patient and primary care provider conversation. The Gail Risk Score may underestimate risk in patients with a family history of certain types of cancer. Expanded risk questions should be asked which also identify those who would benefit from a High Risk program. During High Risk evaluations, a personalized surveillance plan for prevention and detection of breast cancer is developed.

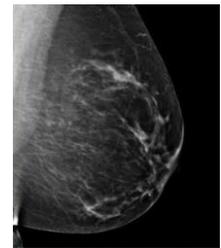
RISK FACTORS FOR BREAST CANCER:

- 1.** The main risk factor for developing breast cancer is simply being a woman.
- 2.** The risk of developing breast cancer increases with increasing age.
- 3.** Genetic: about 5-10% of breast cancers are hereditary (gene mutations BRCA-1 and BRCA-2))
- 4.** Breast cancer is higher among women who have 1st degree relative with breast cancer (mother, sister or daughter)
- 5.** Personal history of breast cancer: 3 to 4 fold increase risk of a new cancer.
- 6.** Race: Caucasians are slightly more likely to develop breast cancer than African-American women, but African-American women are more likely to die of breast cancer.
- 7.** Dense breast tissue may be associated with an increased risk of breast cancer: A number of factors can affect breast density, such as age, menopausal status, hormone therapy, pregnancy and genetics.
- 8.** Previous chest wall radiation during childhood or as a young adult causes a significant increased risk for breast cancer.
- 9.** Benign conditions such as proliferative lesions can raise a woman's risk 1.5 to 2 times normal.
- 10.** Proliferative lesions with atypia can increase risk 3½ to 5 times higher than normal.
- 11.** Lobular carcinoma in situ has a 7 to 11 fold increased risk of developing cancer in either breast.
- 12.** Women with menstrual periods that begin early (before age 12) or ended after age 55 have a slightly higher risk due to longer lifetime exposure to hormones.
- 13.** Lifestyle-related risk factors include: Combined hormone replacement therapy, consumption of more than 1 alcoholic drink a day, being overweight or obese, lack of physical activity

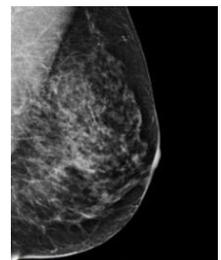
Breast Tissue



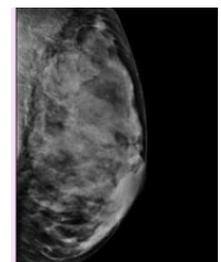
Breast is almost all fatty tissue.



Some glandular and fibrous tissue present.



More glandular and fibrous tissue present. This can make it hard to see small masses.



Breast is almost all glandular and fibrous. A small mass could be missed here.

CONTINUED ON NEXT PAGE

EXPANDED RISK QUESTIONS WOULD INCLUDE:

- Do you have a personal or family history of ovarian cancer?
- What is the number of aunts/cousins/grandmothers with breast cancer?
- Have you or any family member (maternal or paternal) had:
 - *More than one cancer diagnosis in a single person?*
 - *Male breast cancer?*
 - *Eastern European (Ashkenazi) Jewish ancestry?*
 - *Known cancer gene mutation in your family? (BRCA 1, 2 or HNPCC/Lynch genes, or others).*

SHOULD ADDITIONAL IMAGING BE PURSUED IN WOMEN WITH DENSE BREAST TISSUE?

The recommendations for screening mammography are exactly the same for women with dense breasts as for the rest of the population. Mammography is the only screening modality that has undergone randomized controlled trials demonstrating a reduction in breast cancer mortality. There is no recommendation that it be replaced with another test in any subset of the population. For patients who are interested in additional screening options, a breast cancer risk assessment is appropriate. It is a good starting point in the discussion of whether supplemental tests will be beneficial and what tests, if any, to order.

Digital Breast Tomosynthesis (commonly referred to as 3D mammography) is a cutting edge technology now available in Kent County. This technology produces a conventional 2D mammogram which has been the 'gold' standard for breast imaging, while also acquiring images of individual layers of breast tissue which can be viewed as an aggregate, diminishing the masking effect of dense breast tissue, compared to the 2D image. This technology allows the radiologist to more accurately distinguish normal fibroglandular tissue from an underlying mass.

Three major studies have shown tomosynthesis to have a 40-50% higher cancer detection rate than conventional mammography, especially in the setting of dense breasts. Studies have also shown a 5.7/1000 cancer detection rate with tomosynthesis versus 3.8/1000 with conventional mammography. Another benefit to the patient is tomosynthesis dramatically reduces the number of cases that need to be 'called back' for additional imaging.

"3D mammography helps in the setting of dense breasts. It reduces the chances of screening patients having to come back for additional views and improves our cancer detection for masses in dense breasts." according to Jamie Caughran, MD, Medical Director at the Mercy Health Comprehensive Breast Center in Grand Rapids.

The radiation dose is the same as a conventional mammogram if the system has the ability to digitally recreate the traditional 2-view mammograms. The absorbed radiation dosage for a conventional mammogram is .86 mGy which is the equivalent of air travel coast to coast. Not all tomosynthesis units recreate the traditional 2-view mammogram, so radiation doses may be slightly higher at some locations. The patient experience during tomosynthesis is identical to a traditional mammogram, or may even be less uncomfortable as it requires slightly less compression.

Insurance coverage for 3D mammography is variable as it is a new technology. As of January 1, 2015, Priority Health and Medicare are covering diagnostic as well as screening. 3D is often performed as part of a diagnostic evaluation for a mass or known imaging finding. Asymptomatic patients for whom 3D would be most appropriate include:

- Patients with prior mammograms read as 'heterogeneously dense' or 'extremely dense' breasts, (category C or D.)
- Patients who are high risk for developing breast cancer.
- Patients who have strong desire to pursue screening 3D but do not fulfill either of these criteria.

For those patients whose insurance carrier does not cover 3D yet, most breast centers have reduced the out-of-pocket charge for this imaging of approximately \$150 (insurance is billed for the screening 2D mammography).

The other breast imaging "screening options" include screening MRI and ultrasound. Screening breast MRI has been shown to substantially increase the rate of cancer detection. It is recommended in patients who are at very high risk (>20% lifetime risk) based on American Cancer Society guidelines. For patients at "intermediate risk," such as those with a personal history of breast cancer or a prior biopsy diagnosis of atypia (equivalent to a 15% to 20% lifetime risk), a patient-centered shared decision-making approach is recommended.

Additional resources
are available at
www.breastdensity.info

Whole breast ultrasound is not currently recommended by the American Cancer Society as a screening tool and therefore ultrasound is currently used mainly as an adjunct to mammography and to evaluate palpable lumps. As a screening tool, ultrasound is an out of pocket expense for patients. The interpretation of hand-held ultrasound images by experienced radiologists leads to an accuracy close to 100% for differentiating simple cysts from other lesions,

and can improve distinction of malignant from benign breast masses. Volume Scanning (ABVS)—or whole breast ultrasound—is currently being investigated as a means to reduce ultrasound breast examination time, measure additional tissue properties, and provide 3D volumes that can be reviewed post-examination. When compared to hand-held ultrasound, 3D-AUS has been found to provide similar image quality and diagnostic information, BI-RADS ratings, and mass detection rates. Studies have shown a modest increase in cancer detection with breast ultrasound, but also a high rate of false positives resulting in benign biopsies. Also, patients should be aware that mammography detects breast some cancers that are not visible on ultrasound, and ultrasound should not replace screening mammography. Screening breast ultrasound may be a reasonable option for patients with dense breasts who desire additional imaging to supplement mammography. The choice to have this test should be made on an

individual basis after a discussion of these risks, benefits, and costs.

In summary, there is currently no defined additional test/step recommended for women with dense breasts who are at average risk for developing breast cancer. To date, mammography is the only screening modality that has undergone randomized controlled trials demonstrating a reduction in breast cancer mortality. Tomosynthesis (3D mammogram), is an advanced, cutting-edge mammography technology shown to have significantly improved sensitivity in detecting breast cancer, particularly in dense breast tissue, while decreasing false positive rates compared to conventional 2D mammography alone. For patients who are interested in additional screening options, a breast cancer risk assessment is appropriate. It is a good starting point in the discussion of whether supplemental tests will be beneficial and what tests, if any, to order.



More Information

For more information on breast density or advanced screening, visit www.kcms.org

BREAST DENSITY, BREAST CANCER RISK, AND CALIFORNIA

Scenarios for Clinicians

The California Breast Density Information Group (CBDIG) is a working group of breast radiologists and breast cancer risk specialists, representing academic and community-based practices across California. The group was formed to assist patients, referring doctors, and radiologists in responding to new legislation in California (SB-1538) that will mandate radiologists report breast density to patients. Below are scenarios on how clinicians may respond to patient's questions about mammograms and breast density.

SCENARIO

My patient received the letter stating she has dense breasts. Now she is wondering whether she should continue to get mammograms at all.

She should continue to get screening mammograms. The breast density law does not reflect any change in the current mammography screening recommendations by professional medical societies. Mammograms have been shown to be effective in lowering breast cancer mortality for all breast densities.

SCENARIO

My patient received the new breast density letter. She is concerned because she now thinks she is at high risk for breast cancer.

Reassure the patient that breast density alone has only a small impact on breast cancer risk.

She wants to know specifically how it changes her risk.

Look up her mammogram report (different from the patient letter).

1. If the report states her density is heterogeneously dense, this is associated with minimal risk above average (RR=1.2 compared to average breast density).
2. If her density is extremely dense (also sometimes called simply dense), this factor doubles her risk of breast cancer compared to average density, similar to the risk associated with a family history of breast cancer in a mother, sister, or daughter. For example, having extremely dense tissue on its own raises the 10-year risk of breast cancer in the average 50 year old woman from 1 in 42 to 1 in 21.

California Breast Density Information Group (CBDIG)

Stanford University
School of Medicine
Debra M. Ikeda, MD
Jafi A. Lipson, MD
Bruce L. Daniel, MD
Allison Kurian, MD MSc

University of California, Davis
Karen K. Lindfors, MD
Jonathan Hargreaves, MD
Donna D. Walgenbach, MS CGC
Elyse Love, MS CGC

University of California, Irvine
Stephen Feig, MD

University of California,
San Diego
Haydee Ojeda-Fournier, MD

University of California,
San Francisco
Bonnie N. Joe, MD PhD
Edward A Sickles, MD
Elissa R. Price, MD
Lauren Ryan, MS LCGC

University of California,
Los Angeles
Lawrence Bassett, MD
Alta-Bates Summit Medical
Center
R. James Brenner, MD JD

California Pacific Medical Center
Jessica W. T. Leung, MD

SCENARIO

My patient received the new breast density letter. She wants to be screened with another modality instead of mammograms.

Explain that at this point in time, there is no other method that is recommended to replace the mammogram. There are certain manifestations of cancer (for example, calcifications) that are only seen on mammography. The other “screening options” referred to in the letter are in addition to, and not instead of, a routine screening mammogram.

SCENARIO

My patient received the new breast density letter. She wants to get additional tests to be screened for breast cancer.

Does she have a first degree relative (mother, sister, daughter) who had premenopausal breast or ovarian cancer, or a male relative with breast cancer?

or

Does she have a history of atypia (ADH, ALH) or LCIS on a previous breast biopsy?

Yes: She would likely benefit from a breast cancer risk assessment. This could be performed by a physician with experience in breast cancer risk model selection and interpretation, or by a cancer risk assessment program.

No: If the patient does not have other breast cancer risk factors, reassure her that her risk remains low. Educate the patient about the risks and benefits of screening MRI and ultrasound (higher cancer detection, but also higher false positive biopsy rates and short term follow-up recommendations). Many health centers have chosen not to offer screening breast ultrasound, in part because ultrasound depicts many fewer mammographically invisible cancers than does screening MRI. Tomosynthesis is an additional screening test with current results suggesting some increase in cancer detection and decreased false positives.

Explain that at most medical centers, additional screening tests are an out-of-pocket cost for the patient, unless they have been assessed to have high risk. Assist the patient in making the best personal choice to meet her needs based on these factors, using a shared decision making process.

CONTINUED ON NEXT PAGE



SCENARIO

My patient has “heterogeneously dense” or “extremely dense” breasts and she also has other risk factors. She has completed a risk assessment showing her overall risk to be high (e.g. calculated >20% lifetime risk or >5% 10-year risk), or has a BRCA mutation or history of mantle radiation.

Recommend annual breast MRI and annual mammogram for screening. Screening breast MRI is typically covered by insurance for high-risk women. If a woman is being screened annually with MRI and mammogram, no additional screening tests (such as ultrasound) are needed. Encourage referral to formal high risk program which will manage additional imaging and risk reduction strategies.

SCENARIO

My patient has “heterogeneously dense” or “extremely dense” breasts and she also has other risk factors. She has completed a risk assessment showing her overall risk to be high (e.g. calculated >20% lifetime risk or >5% 10-year risk).

I recommended an annual MRI, but the patient has either claustrophobia, pacemaker, contrast allergy, limited insurance coverage plan, or other reasons why she does not want to have an MRI.

Recommend screening ultrasound as the second-best supplementary screening test for high risk women. Studies have shown some utility for ultrasound in high risk women if screening MRI is not performed.

References

- American College of Radiology. Breast Imaging Reporting and Data System® (BI-RADS®) 5. Reston, Va: American College of Radiology; Anticipated 2013.
- Berg WA, Blume JD, Cormack JB, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *JAMA : the journal of the American Medical Association* 2008;299:2151-63.
- Berg WA, Zhang Z, Lehrer D, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *JAMA : the journal of the American Medical Association* 2012;307:1394-404.
- Bevers TB, Anderson BO, Bonaccio E, et al. NCCN clinical practice guidelines in oncology: breast cancer screening and diagnosis. *Journal of the National Comprehensive Cancer Network : JNCCN* 2009;7(10):1060-96.
- Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. *The New England journal of medicine* 2007;356:227-36.
- Buist DS, Porter PL, Lehman C, Taplin SH, White E. Factors contributing to mammography failure in women aged 40-49 years. *Journal of the National Cancer Institute* 2004;96:1432-40.
- Carney PA, Miglioretti DL, Yankaskas BC, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. *Annals of internal medicine* 2003;138:168-75.
- Hooley RJ, Greenberg KL, Stackhouse RM, Geisel JL, Butler RS, Philpotts LE. Screening US in patients with mammographically dense breasts: initial experience with Connecticut Public Act 09-41. *Radiology* 2012;265:59-69.
- Kelly KM, Dean J, Comulada WS, Lee SJ. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. *European radiology* 2010;20:734-42.
- Kuhl C, Weigel S, Schrading S, et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2010;28:1450-7.
- Mainiero MB, Lourenco A, Mahoney MC, et al. ACR Appropriateness Criteria Breast Cancer Screening. *Journal of the American College of Radiology : JACR* 2013;10:11-4.
- Pinsky RW, Helvie MA. Mammographic breast density: effect on imaging and breast cancer risk. *Journal of the National Comprehensive Cancer Network : JNCCN* 2010;8:1157-64; quiz 65.
- Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA: a cancer journal for clinicians*. 2007;57(2):75-89.
- Schousboe JT, Kerlikowske K, Loh A, Cummings SR. Personalizing mammography by breast density and other risk factors for breast cancer: analysis of health benefits and cost-effectiveness. *Annals of internal medicine* 2011;155:10-20.
- Sickles EA. The use of breast imaging to screen women at high risk for cancer. *Radiologic clinics of North America* 2010; 48:859-878.
- Skaane P, Bandos AI, Gullien RT, et al. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. *Radiology* 2013; Epub ahead of print.
- Smith RA, Brooks D, Cokkinides V, Saslow D, Brawley OW. Cancer screening in the United States, 2013. *CA : A cancer journal for clinicians* 2013; Epub ahead of print.
- Tice JA, Cummings SR, Smith-Bindman R, Ichikawa L, Barlow WE, Kerlikowske K. Using clinical factors and mammographic breast density to estimate breast cancer risk: development and validation of a new predictive model. *Annals of internal medicine* 2008;148:337-47.
- Vachon CM, van Gils CH, Sellers TA, et al. Mammographic density, breast cancer risk and risk prediction. *Breast cancer research : BCR* 2007;9:217.
- van Gils CH, Otten JD, Verbeek AL, Hendriks JH. Mammographic breast density and risk of breast cancer: masking bias or causality? *European journal of epidemiology* 1998;14:315-20.
- Whitehead J, Carlile T, Kopeccky KJ, et al. Wolfe mammographic parenchymal patterns. A study of the masking hypothesis of Egan and Mosteller. *Cancer* 1985;56:1280-6.