Breast Tissue Density, Cancer Risk, and State Patient Notification Laws

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- Breast tissue density determination
- Density and increased cancer risk
- Density and masking effect
- State laws regarding patient notification
- Education/outreach to patients & providers

In other words,

- What is breast density?
- Why is it important?
- What to do about it?

- Breast tissue density determination
- Density and increased cancer risk
- Density and masking effect
- State laws regarding patient notification
- Education/outreach to patients & providers

What is breast density?

Density = how much of the breast is occupied by fibroglandular tissue

- A radiographic (mammographic) assessment
- May be expressed qualitatively (description) or quantitatively (percentage)

Contributors to breast density determination

- White on mammogram (Radiopaque, Dense)
  - Glandular tissue
  - Fibrous/stromal tissue
  - Most masses
- Black on mammogram (Radiolucent, Not dense)
  - Fatty tissue

Density is most often estimated based on 2-D projections (CC, MLO)

- Some challenges affecting density determination
  - Anatomy (e.g., central fat within shell of glandular tissue)
  - Positioning
  - Compression
  - Exposure Technique

Kopans DB. *Radiol* 2008; 246(2): 348-353

Subjectivity in Density Assessment

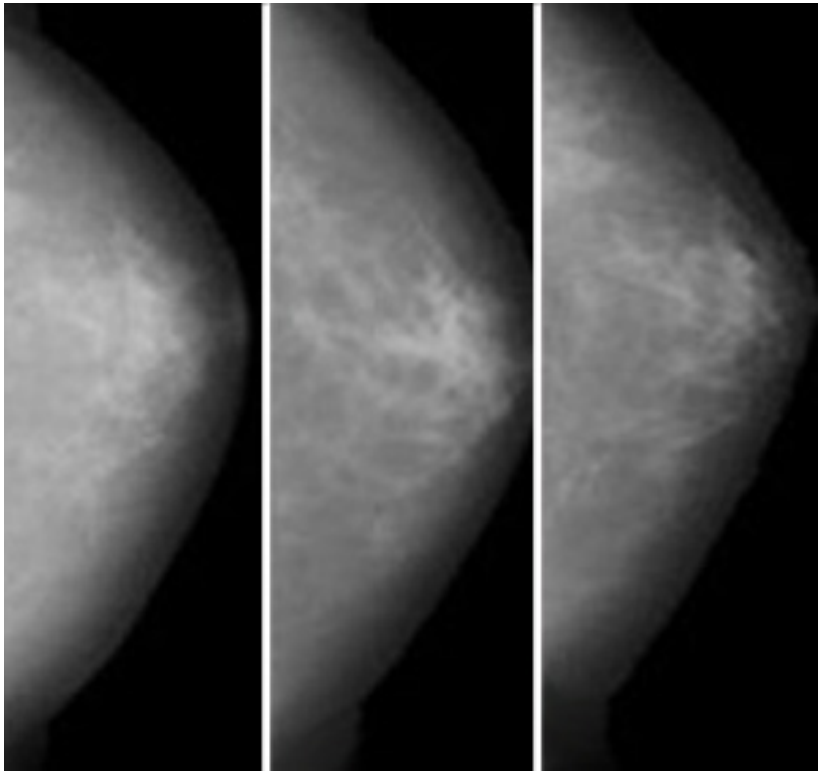
"There is wide variation in density assessment across radiologists... The likelihood of a woman being told she has dense breasts varies substantially according to which radiologist interprets her mammogram."

Sprague BL et al. *Ann Int Med* 2016. doi: 10.7326/M15-2934
Publ. online 19 July 2016

Some causes of increased density

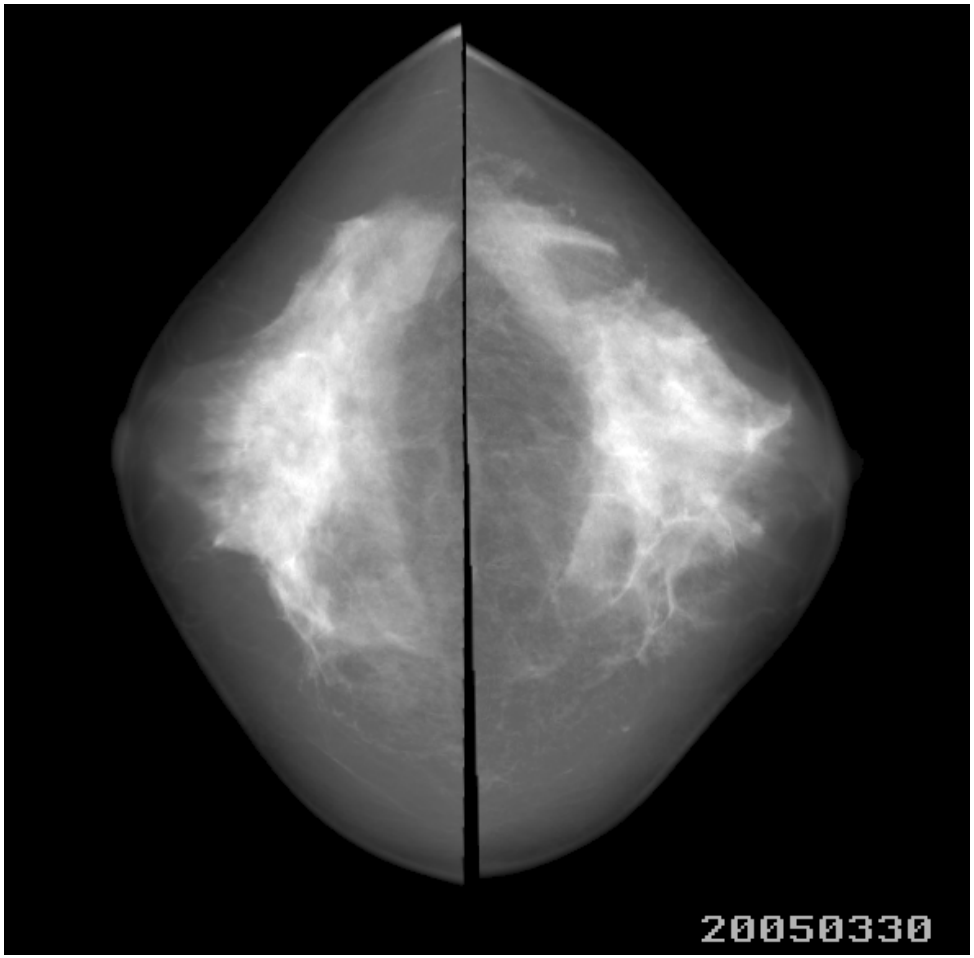
- Younger age
- Pregnancy, breast-feeding
- Fibrocystic changes
- Hormonal influence, incl. menstrual cycle
- Hormone replacement therapy
- Weight loss
- Antipsychotic medications
- Breast masses

Density can vary over time



http://www.mayo.edu/research/mammography-health-study

Density can vary over time

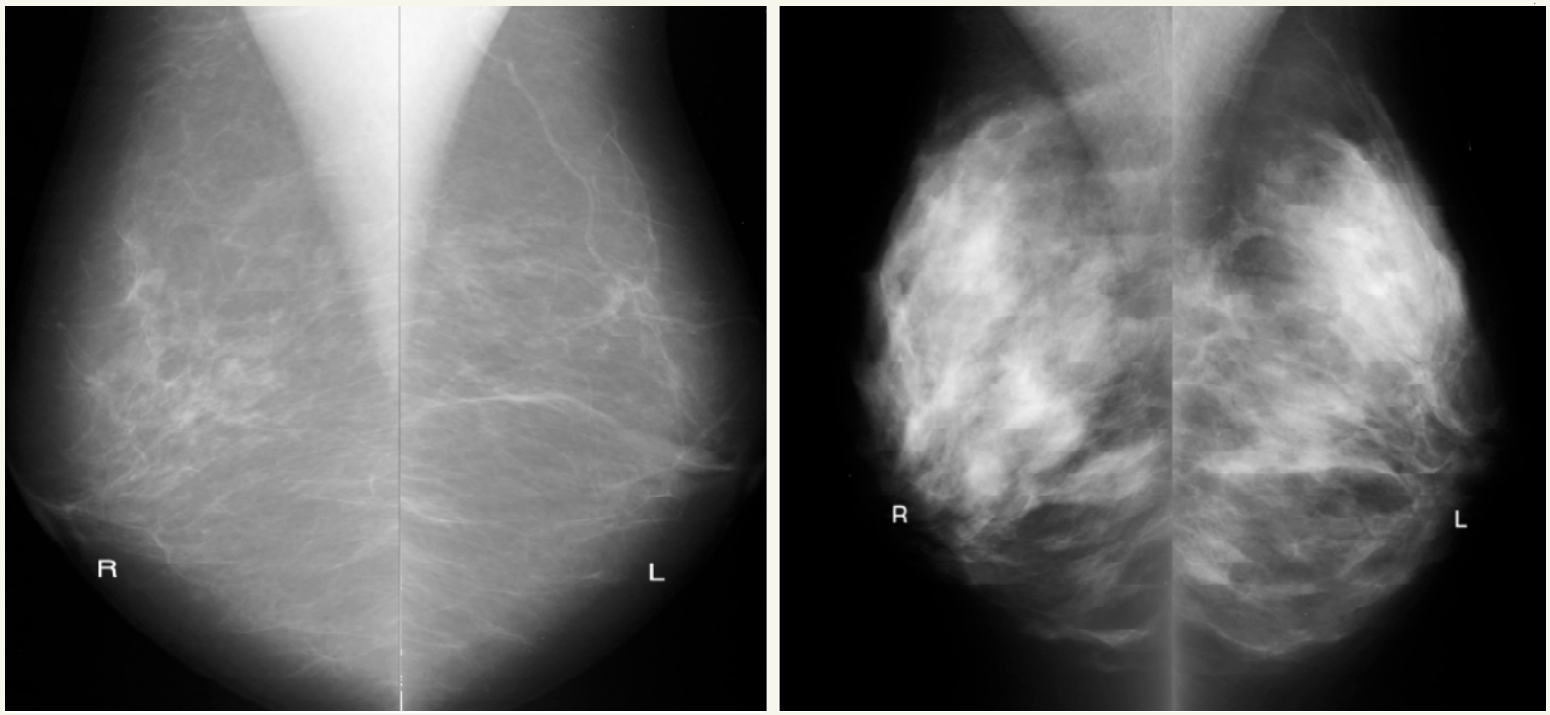


www.understandbreastdensity.org

Effect of hormone therapy

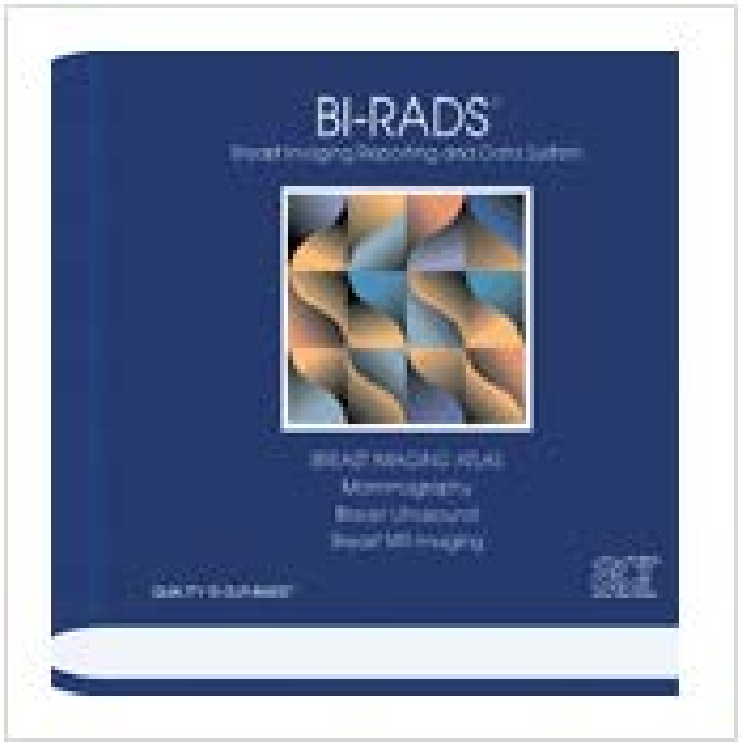
Before hormone therapy

After 1 yr of hormone therapy



Ghosh K, Vachon C. *Menop Med* 2010; 18: 34-40

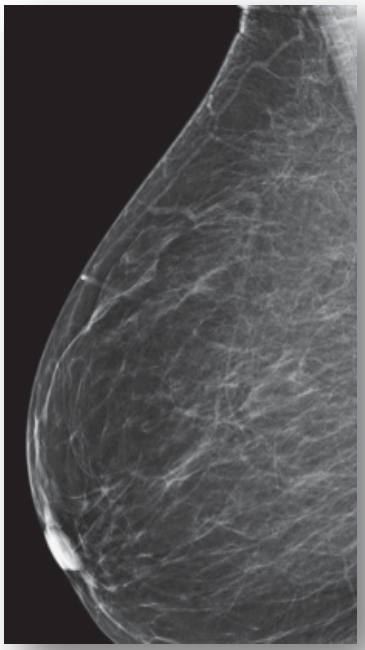
ACR BI-RADS



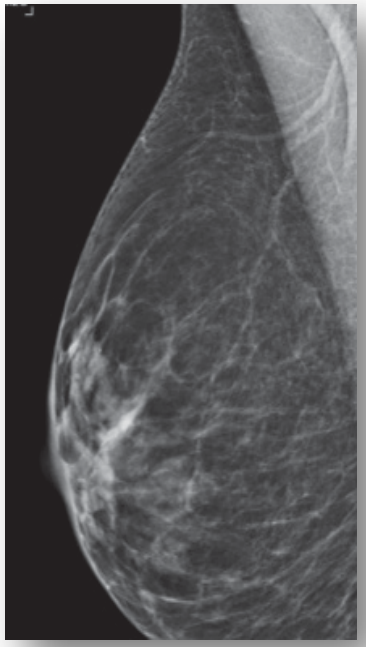
4th Ed., 2003

5th Ed., 2013

Images courtesy of ACR

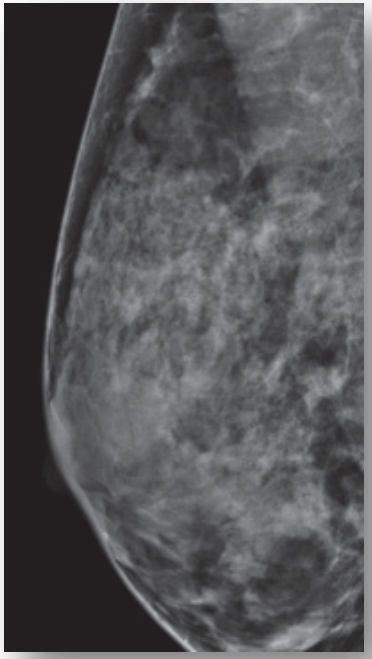


Almost entirely fatty



Scattered areas of fibroglandular density

Heterogeneously dense



Extremely dense

Images courtesy of ACR

2003 BI-RADS® Atlas (4th Edition)	2013 BI-RADS® Atlas (5th Edition)
1. The breast is almost entirely fat (<25% glandular) 2. There are scattered fibroglandular densities (approximately 25% - 50% glandular) 3. The breast tissue is heterogeneously dense, which could obscure detection of small masses (approximately 51% - 75% glandular) 4. The breast tissue is extremely dense. This may lower the sensitivity of mammography (>75% glandular)	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 (Quartiles have been eliminated)

In 5th Edition:

- No quartiles, just descriptions
- Letters rather than numbers for categories

http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/BIRADS/BIRADS%20V5%20Changes

Breast density distribution among US women

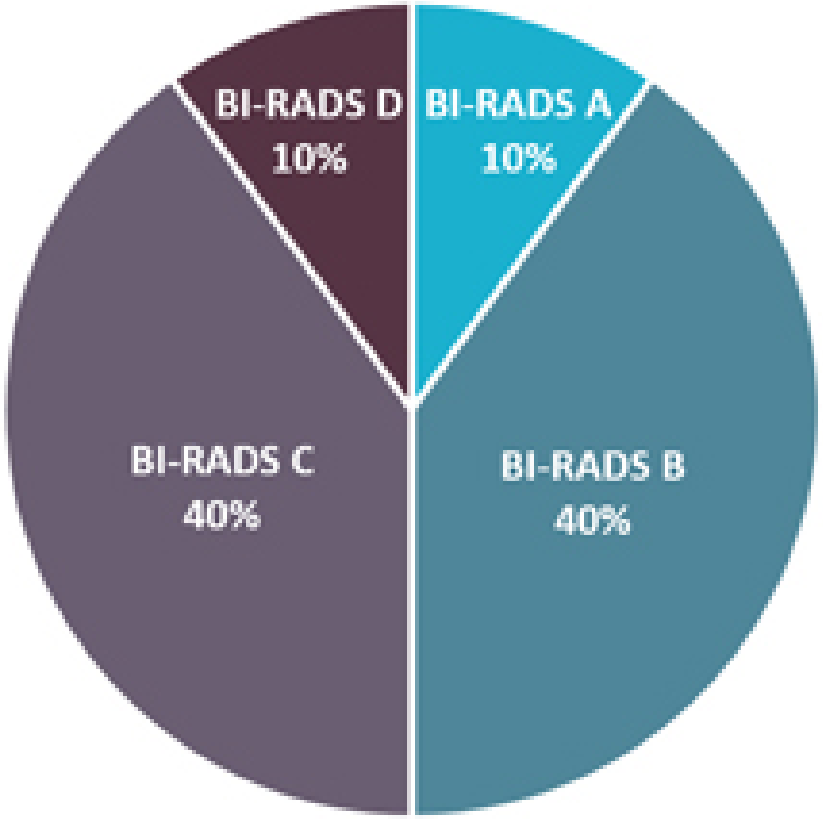
- 10% Almost entirely fatty
- 40% Scattered areas of fibroglandular density
- 40% Heterogeneously dense
- 10% Extremely dense

Breast density distribution among US women

- 10% Almost entirely fatty
- 40% Scattered areas of fibroglandular density
- 40% Heterogeneously dense*
- 10% Extremely dense*

*These two latter categories are typically grouped together as *dense*, so the term *dense* covers 50% of women

Breast density distribution among US women



Quantitative assessment of density

- Various 2-D and 3-D techniques proposed
  - Volumetric analysis of digital mammogram
  - Dual-energy mammography
  - Digital breast tomosynthesis
  - CT
  - MRI
  - Whole-breast ultrasound (US)

Quantitative assessment of density

- Either under research or in limited use
- Density measurements vary between modalities

Tagliafico A et al. *Br J Radiol* 2013; 86: 20130528

- Quantitative density measurements tend to be lower than assessments made by visual estimation

Martin KE et al. *Radiol* 2006; 240(3): 656-665
Shivani P et al. *Indian J Radiol Img* 2015; 25(4): 391-396

Why is density important?

Why is density important?

- At least 2 reasons

- Breast tissue density determination
- Density and increased cancer risk
- Density and masking effect
- State laws regarding patient notification
- Education/outreach to patients & providers

Density is an independent risk factor for breast cancer

- Greater density = greater risk (up to 3-6x)
- Effect is greatest at extremes

≥50% dense vs. 10% dense: 3.39x risk

Yaghjyan L et al. *JNCI* 2011; 103: 1179-1189

≥75% dense vs. 10% dense: 4.7x risk

Boyd NF et al. *NEJM* 2007; 356: 257-236

Some proposed explanations for increased risk

- Reason(s) not known definitively
- Density may reflect level of hormone exposure
  - Endogenous or exogenous
- Greater density = more glandular cells
  - More cells subject to possible cancer development

No evidence that density leads to increased mortality

- "High mammographic breast density was not associated with risk of death from breast cancer"

Gierach *JNCI* 2012; 104: 1218-1227

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Contributors to breast density determination

- White on mammogram (Dense)
  - Glandular tissue
  - Fibrous/stromal tissue
  - Most masses
- Black on mammogram (Not dense)
  - Fatty tissue

Dense tissue can hide cancers

- “Masking effect”
- A known limitation of mammography
- Some patients, especially if high-risk, may benefit from additional imaging such as DBT, US, MRI
- However, supplemental screening can also increase false positives

What are some clinical approaches to dense breasts?

Patient evaluation may include

- Individual risk assessment
- Monthly breast self-exam?
- Annual clinical breast exam by HCP
- Annual mammography – some studies show that, for dense breasts:
  - Digital is more sensitive/accurate than screen-film

    Pisano ED et al. *NEJM* 2005; 353(17):1773-1783
    Kerlikowske K et al. *Ann Int Med* 2011; 155(8):493-502
  - DBT is better than 2D mammography

    Destounis SV et al. *AJR* 2015; 204: 261-264

Some clinical options if breasts are dense

- Women with average risk may not need further screening imaging
- If warranted, supplemental screening imaging of dense breasts may include
  - Another mammographic modality
  - Screening ultrasound
  - Screening MRI (e.g., if high genetic risk, or history of cancer)
  - Nuclear medicine exams (PEM, BSGI)

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State legislation

- Encouraged by patient advocacy
- 27 States (thus far) now have laws mandating patient notification of density
- Of these 27, most require a prescribed text, but texts vary from State to State

Example of State notification

- *Alabama*: Your mammogram shows that your breast tissue is dense. Dense breast tissue is very common and is not abnormal. However, dense breast tissue may make it harder to find cancer on a mammogram and may also be associated with an increased risk of breast cancer. This information about the result of your mammogram is given to you to raise your awareness. Use this information to talk to your doctor about your own risks for breast cancer. At that time, ask your doctor if more screening tests might be useful, based on your risk. A report of your results was sent to your physician.

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Some variations among State texts

- Notification to all patients vs. only to dense patients
- Conditional vs. definite
- Fraction or % of US women with dense tissue
- Density as risk factor for breast cancer

Some variations in State laws

- Notification + separate explanatory paragraph, vs. one combined paragraph
- Some apply to different levels of density (heterogeneously + extremely dense; only extremely dense; or “dense”)
- Also differ on the party responsible for notification - interpreting physician vs. mammography facility

Proposed Federal legislation

- H.R. 716 and S. 370, Breast Density and Mammography Reporting Act of 2015
- Referred to Health Committee (Senate)/ Subcommittee (House)
- If enacted, would amend MQSA

Proposed Federal legislation

- H.R. 716 and S. 370 propose that patients be told:
  - Information about breast density
  - The effect of density in masking cancer, based on the patient's breast density
  - To speak with their physician regarding any questions and whether they would benefit from additional tests

Current Federal legislation

- Mammography Quality Standards Act (MQSA) requires certain communication between interpreting physician, referring physician/HCP, and patient
- MQSA requirements are detailed in the implementing regulations

MQSA Regulations

Under current regulations:

- Report must be sent to referring provider, and lay summary to patient
- Report to referring provider must include certain items (e.g., Final Assessment, Recommendations)
  - Reporting breast density is not required
- Summary of report in lay language must be sent to patient

MQSA Regulations

- National Mammography Quality Assurance Advisory Committee (NMQAAC) meeting, November 2011
- Reached a consensus to require reporting of breast density in reports to HCPs and lay summaries to patients

MQSA Regulations

- FDA intends to propose amendments to MQSA regulations
- Any proposed amendments will be published and open for public comment
- Any proposed amendments are expected to address the issue of breast density notification

Federal vs. State legislation

- Only a few States with density legislation specify that their law would be superseded by any future Federal density legislation
- Relationship of most States' notification laws to any future Federal density legislation is unclear
- MQSA does allow States to have "more stringent" requirements than the Federal standards

Considerations in notification

- General consensus that patients are entitled to know their medical information and risk factors
- Density notification promotes informed and shared decision-making
- However, any further decisions also depend on other individual risk factors
- Some patients may benefit from supplemental screening

Considerations in notification

- Supplemental screening incurs added costs to patient and health care system
  - Only a few States mandate insurance coverage of supplemental screening
- Supplemental screening may find additional cancers, but also carries risks of false positives, further workup (imaging/ biopsy), anxiety, pain

Considerations in notification

From NMQAAC 2011 Summary:

"The committee members were in general agreement on requiring reporting breast tissue density in reports and lay summaries..."

Considerations in notification

Caveats in NMQAAC 2011 Summary:

"… but several members did express concerns about what constitutes a dense breast and what recommendations might be made in advising physicians and patients on what to do with the information…"

Considerations in notification

Caveats in NMQAAC 2011 Summary:

"…The committee did not reach a consensus in the professional community on the magnitude of the risk that having dense breasts confers on patients or the best way to further evaluate these patients through the use of alternative imaging modalities."

Considerations in notification

- Since 2011, greater scientific consensus on
  - Defining dense breasts as heterogeneously dense + extremely dense (BI-RADS c + d)
  - Degree of risk of breast cancer conferred by density
- Availability of more supplemental screening methods
- More information available on how to choose supplemental screening tools based on patient's individual risks

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Education/outreach to patients from

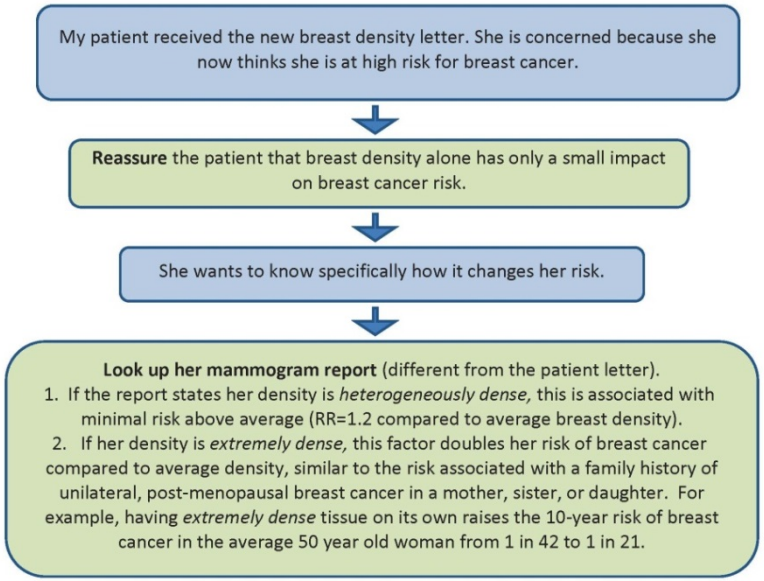
- Medical/Scientific Organizations
- Industry
- Interpreting Physicians
  - Newsletters
  - Interviews in Lay Press
  - Other Educational Materials
  - Public Lectures/Presentations

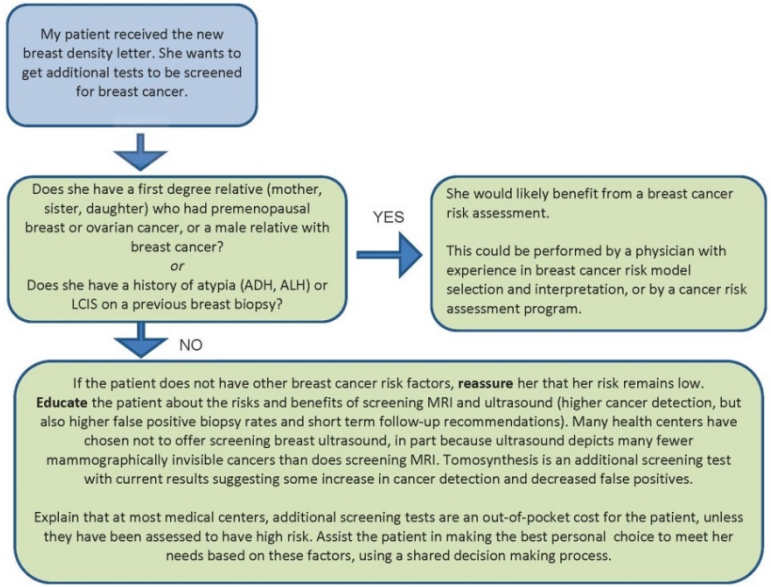
Education/outreach to Referring HCPs from

- Professional organizations
- CME providers
- Journal articles
- Clinical decision aids

Example of Clinical Decision Aid:

Calif. Breast Density Info. Grp. *Scenarios for Clinicians*





http://www.breastdensity.info/docs/DENSITY-SCENARIOS-FOR-CLINICIANS.pdf

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Discussion

FDA is seeking input from the Committee on how facilities, referring health care providers, and patients are responding in States that have density notification requirements.