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.”

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
Almost entirely fatty

Scattered areas of fibroglandular density

Heterogeneously dense

Extremely dense

Images courtesy of ACR
In 5th Edition:
- No quartiles, just descriptions
- Letters rather than numbers for categories

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


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

Martin KE et al. Radiol 2006; 240(3): 656-665
Why is density important?
Why is density important?

• At least 2 reasons
• Breast tissue density determination

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Density is an independent risk factor for breast cancer

- Greater density = greater risk (up to 3-6x)
- Effect is greatest at extremes
  \[ \geq 50\% \text{ dense vs. } 10\% \text{ dense}: 3.39x \text{ risk} \]
  Yaghjyan L et al. *JNCI* 2011; 103: 1179-1189
  \[ \geq 75\% \text{ dense vs. } 10\% \text{ dense}: 4.7x \text{ risk} \]
  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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  - 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
  - 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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• Education/outreach to patients & providers
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.
Content 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

- 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 & providers
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:

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, this factor doubles her risk of breast cancer compared to average density, similar to the risk associated with a family history of unilateral, post-menopausal 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.

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.

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.