Supplemental Breast Imaging to Improve Screening in Women with Dense Breasts

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Disclosures

NA
Objectives

1. Define and assess mammographic breast density
2. Clinical implications of breast density
3. Current strategies for supplemental screening
4. Future directions
Defining Mammographic Breast Density

• Amount or proportion of fibro glandular tissue (FGT) relative to fatty tissue

• FGT = breast glands and ducts; origin of most breast cancers (BC)

• Visually assessed, with focus on “masking”

• Per ACR BI-RADS atlas, binned into 4 categories:
  A. The breasts are almost entirely fatty
  B. There are scattered fibro glandular densities
  C. The breasts are heterogeneously dense, which may obscure small masses
  D. The breasts are extremely dense, which lowers the sensitivity of mammography
Breast Density

- Pectoralis Muscle
- Fat (dark gray)
- Fibroglanular Tissue (white)
Breast Density

- Fatty: 10%
- Scattered: 40%
- Heterogeneously Dense: 40%
- Extremely Dense: 10%
Breast Density: What Impacts It?

- Genetics

- Endogenous hormones: age, menopausal status, pregnancy/lactation

- Exogenous hormones: HRT, anti-estrogen therapy (Tamoxifen)
Breast Density: Implications

1. Decreased Sensitivity

- Masking
- Sensitivity in fatty breasts: 86-89%
- Sensitivity in extremely dense breasts: 40s-60s%
- Larger tumor size and worse prognosis at diagnosis in dense breasts
Breast Density: Implications

- Decreased Sensitivity: Masking

Edmonds et al, Seminars 2023
Digital Breast Tomosynthesis

• Low dose images obtained as xray tube moves in arc, and reconstructed to create a volume rendering

• FDA approved in 2011, now mammography standard of care

• Can mitigate masking due to 3D reconstruction

• Studies show reductions in screening recall rates

• Increased cancer detection rate (CDR) by 1.2 to 2.7 / 1000

• Unclear impact on CDR in women with dense breasts (particularly extremely dense breasts)

Rafferty 2016; Ciatto 2013; Conant 2014; Haas 2013; Edmonds et al, Seminars 2023
Breast Density: Implications

2. Increased Cancer Risk

- Women with extremely dense breasts have twice the risk of “average density,” four-six times the risk of fatty breasts
- Increased risk of all breast cancer subtypes
- Dense tissue associated with increased risk of invasive disease, larger tumor size at diagnosis
Supplemental Screening:

- Who may need supplemental screening?
- What test should be done for supplemental screening?
If NOT dense: “Breast tissue can be either dense or not dense. Dense tissue makes it harder to find breast cancer on a mammogram and also raises the risk of developing breast cancer. Your breast tissue is not dense. Talk to your healthcare provider about breast density, risks for breast cancer, and your individual situation.”

IF dense: “Breast tissue can be either dense or not dense. Dense tissue makes it harder to find breast cancer on a mammogram and also raises the risk of developing breast cancer. Your breast tissue is dense. In some people with dense tissue, other imaging tests in addition to a mammogram may help find cancers. Talk to your healthcare provider about breast density, risks for breast cancer, and your individual situation.”
Supplemental Screening Options

- Ultrasound/Automated Breast Ultrasound (most utilized to date)
- Contrast Enhanced Breast MRI (standard or abbreviated protocol)
- Contrast enhanced digital mammography
- ACR Appropriateness Criteria: all three “may be appropriate” in women with average risk and dense breasts
Screening Breast Ultrasound

• PROS:
  - Incremental CDR of 2.0-2.7 / 1000 in women w/ dense breasts (2.3 / 1000 across studies)
  - Majority are invasive, node negative

• CONS
  - Notably increased rates of recall, follow-up imaging and biopsy recs, AND decreased positive predictive value of biopsy (ACRIN 6666)
  - Absolute increase in recalls: 7.5%
  - 8.6% BIRADS 3 rate, vs 2.2 for mammo
  - Time/labor intensive
  - Extreme user variability

Berg et al, JAMA 2012; Vourtsis et al, Eur Radiol 2019
Screening Breast Ultrasound: Automated Breast Ultrasound (ABUS)

- 65 F, Screening mammogram
- Heterogeneously dense
- BI-RADS 1 (negative) assessment

1:00 axis, 2 cm from the nipple
Screening Breast Ultrasound:
Automated Breast Ultrasound (ABUS)

1:00 axis, 2 cm from the nipple

Stage I Mixed IDC/ILC
MRI: The Gold Standard for Screening

- Highly sensitive (>= 97%)

PROS:
- Performance not affected by breast density
- High cancer detection rates (CDR of 15.5 / 1000 across all densities, avg risk,
- most were sub-cm, node negative, 43% high grade
MRI: The Gold Standard for Screening

• **CONS:**
  - false positives, unnecessary biopsies and follow-up
  - high cost, limited reimbursement in absence of high breast cancer risk
  - long acquisition times
  - claustrophobia

• Many women with access decline MRI
  - 42% women at elevated risk declined MRI (ACRIN 6666)
Abbreviated MRI (ABMR)

- Protocol: single post-contrast sequence, 3-12 mins
- Lower cost
- Increased tolerability and access
- Similar sensitivity (>96) and specificity to full MRI
• 52 F with extremely dense breasts for supplemental screening with 6 mm enhancing mass in the upper central left breast, BIRADS 4, suspicious, on third exam

Edmonds et al, RSNA 2022
Stage I IDC, detected on third AB MR screening study

- Negative screening mammogram 1 month prior
- Stage I Invasive Ductal Carcinoma
Contrast Enhanced Digital Mammography (CEDM)

- Intravenous injection of IV iodinated contrast
- After 2 mins, obtain routine mammographic views with both low and high energy x-rays
- Limited data on CEDM for screening, but studies suggest sensitivity similar to slightly lower than MRI (91 vs 97%)
- Lower cost and shorter exam time compared to MRI
- Preferred by patients over MRI

Potsch et al, Radiology 2022
Phillips et al, Clin Imaging 2017
Contrast Enhanced Digital Mammography (CEDM)

Ghaderi et al, Radiographics 2019
Summary of Techniques to Date:

1. Ultrasound: affordable and accessible; but limited sensitivity and high false positive rates, operator dependent

2. MRI: very high sensitivity; but costly, limited access, and poor patient adherence
   - ABMR decreases cost, scan time

3. CEDM: high sensitivity, preferred over MRI by patients; limited access, still exploratory
Future Directions

1. Automated mammographic textural analysis for incorporation into risk models

2. Novel imaging based biomarkers, including for MRI and PET

3. Novel blood based biomarkers to predict risk

4. Artificial Intelligence:
   Deep Learning for predicting risk based on imaging features, including texture-based
AI: To Better Define Who Needs Supplemental Screening

• Studies of deep learning algorithms to compare traditional breast cancer risk models, like Tyrer Cuzick, to:

A. Risk factor logistic regression based on traditional risks (i.e. family history)
B. Image-only deep learning model
C. Hybrid model- deep learning imaging + traditional risks

Image-based deep learning models, especially those that also incorporate traditional risk factors substantially improve risk assessment over the next 5 years!

Yala et al, Radiology 2019
Summary

Novel approaches are needed to:

• Precisely define who, among the 40-50% of women with dense breasts, need supplemental screening

• How to screen them

• When to screen them

**Closely consider impacts of cost, access, and study populations on health equity and health disparities as we develop both the imaging modalities and the plans for utilization**
Thank you!

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