Breast Density - What's This All About

Pam Fulmer, BA RT (R)(M)(QM)
Fulmer Consulting Group
816-373-3262

What is Mammographic Density

Radiographically the breast consists of two component tissues
- Fibro glandular
  - Mixture of fibrous tissue connective tissue (the stroma) and the functional (glandular) epithelial cells that line the ducts of the breast (parenchyma)
- Fat (Adipose)
  - Has a lower x-ray attenuation coefficient then fibro glandular tissue and therefore is more transparent on an x-ray. It appears darker on an x-ray.

Breast Density in the News

Breast Density in the News

Why is Breast Density Important? - Breast Density Facts

- 40% of women have dense breasts
- X-ray is only 48% effective in dense breasts, compared to 98% in fatty breasts
- Dense breasts are 4-6 more times to develop cancer than fatty breasts
- Breast density is a more significant risk factor than having a mother and sister with breast cancer
- Cancer recurrence is four times more likely in women with dense breasts
- Radiologists only agree on BI-RADS® breast density 60% of the time, some radiologists never classify BI-RADS® A, some rarely classify BI-RADS® D
- Classifications of breast density is highly subjective
- 35+ Years of research with very large number of published papers have documented the importance and difficulty associated with classification of breast density
John Wolfe-1976
- Radiologist that specialized in mammography.
- Refined the XeroMammography Process
- First proposed that there was a strong association between the parenchymal patterns seen in the mammogram and the risk that women would develop breast cancer

Breast Density Percentages
- Population Dependent
- Common Distribution among Western population
  - Fatty Breasts 10%
  - Scattered Densities 40%
  - Heterogeneously Dense 40%
  - Extremely Dense 10%

Four Patterns-Known as Wolfe Grades
- N Pattern- Fatty radiolucent breast-lowest breast cancer risk
- P1 and P2 Patterns- Indicated progressively greater levels of prominence of fibrous tissue surrounding ducts-higher cancer risk
- DY Pattern- Contains dense sheets of fibro glandular tissue and is associated with the highest risk of breast cancer

Breast Density Studies Results
- Breast density is strongly linked to the probability of detection of breast cancer from a mammogram. A cancer in a fatty breast is likely to be found in 98% of cases, whereas a cancer in a dense breast is likely to be found in 48-63% of the cases.
- Breast density has a proven relationship to breast cancer risk. Women with extremely dense breasts are 4-6 times more likely to develop breast cancer compared to women with fatty breasts

Age Association
- Western population
- Approximately half the women over 50 and approximately 3/4 of the women 40-49 have dense breasts
Current Breast Density Classifications

- 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

ACR Statement

- Recognizes that breast density has an impact on mammography screening
- BI-RADS lexicon describes four categories of breast parenchymal densities
- Instructs radiologists to include this information in the medical report
- The ACR would support an FDA mandate that information on breast parenchymal density be included in the report

ACR Considerations-April 2012

"The assessment of breast density is not reliably reproducible. When the same mammogram is interpreted by a different physician or by the same physician on different occasions, differing density can be reported. If these variations are reported to each woman screened on each occasion, it might result in confusion or an impression of the lack of reliability of mammography.

For women with fatty breasts, the reporting of this information may convey a false sense of security about negative mammography results. Even women with fatty breasts may have breast cancer undetected by mammography and may present with a palpable finding. High-risk women should not be complacent and forego recommended Screening MRI because they have fatty breasts.
The significance of breast density as a risk factor for breast cancer is highly controversial. Moreover, there is no consensus that density per se confers sufficient risk to warrant supplemental screening. For women with dense breasts, receipt of breast density information may create undue anxiety about their risk and worry that mammography may have missed a breast cancer."

ACR Stance 4-29-2012

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When the same mammogram is interpreted by a different physician or by the same physician on different occasions, differing density can be reported.

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Dr. Cappello’s History

*Normal mammogram-November 2003
*Physical exam-January 2004
*Her doctor felt a ridge in her right breast
*Sent her for another mammogram and ultrasound
*Negative mammogram and ultrasound revealed a 2.5 cm tumor which was later confirmed to be Stage 3c breast cancer
*February 3, 2004, she was diagnosed with breast cancer

Stage 3C Breast Cancer

Stage 3 cancer means the breast cancer has extended to beyond the immediate region of the tumor and may have invaded nearby lymph nodes and muscles, but has not spread to distant organs. Although this stage is considered to be advanced, there are a growing number of effective treatment options.

Grass Roots Effort

• Nancy M Cappello, PhD-Executive Director and Founder of 'Are You Dense, Inc.'
• Based on her own diagnosis of advanced stage breast cancer in 2004
• Her late stage breast cancer was not found by mammography

Stage 3C

• This stage is divided into three groups: Stage 3A, Stage 3B, and Stage 3C.
• The difference is determined by the size of the tumor and whether cancer has spread to the lymph nodes and surrounding tissue.
Mastectomy
Reconstruction
8 Chemotherapy Treatments
24 Radiation Treatments
Pathology Report confirmed-Stage 3c cancer because the cancer had traveled to her lymph nodes
Eighteen lymph nodes removed and thirteen contained cancer
REMEMBER- a normal mammogram just weeks before

Are You Dense, Inc.

Was formed to inform women of the need to know their own breast density.
With that the “Understanding Breast Density” legislation started.
First state was Connecticut

Breast Legislation in the US is of two basic types

1. Legislation that requires direct notification of breast density in the mammography report that goes to the patient.
2. Legislation that requires insurance companies to pay for screening breast ultrasound for those women judged to have dense breasts.

Missouri Senate passes mammogram notification bill
Updated: 4:02 PM February 06, 2014
JEFFERSON CITY, Mo.
Women with dense breast tissue would have to be notified about the need for additional screenings at their mammograms under legislation passed by the Missouri Senate.
The measure was passed 32-0 by senators on Thursday and it now heads to the House.
Sponsoring Republican Sen. Dan Brown, of Rolla, says mammograms might not pick up cancer if a woman has dense tissue. He says his wife was diagnosed with breast cancer only after a biopsy was taken after several mammograms turned up negative.
Starting in 2015, the bill would require facilities that perform mammograms to notify patients that if they have dense breast tissue that additional tests might be required to detect cancer.
In 2014, House and Senate Chambers Joined Together to Introduce Companion Breast Density Reporting Bills in 2014

As 114th United States Congress begins, Senate and House Due to Reintroduce Breast Density Reporting Bills in 2015

The bill would set a minimum federal standard, as designated by the Secretary of Health and Human Services (HHS), for notification and recommend women discuss with their doctors whether additional screening is necessary. The bill also directs HHS to study improved screening options for women with dense tissue.

ISSUES FACING RADIOLOGISTS-DENSITY

What issues do radiologists face regarding density?

- "Normal" variables that effect image quality can have significant impact on the appearance of breast density

  ✓ Scatter radiation
  ✓ Tube / filter combination
  ✓ Detector material
  ✓ Technique / exposure
  ✓ Compression
  ✓ Positioning
  ✓ Multiple technologists
  ✓ Manufacturer of mammography system
  ✓ Manufacturer (s) image processing
  ✓ Changes in patient breast tissue

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www.understandbreastdensity.org
What issues do radiologists face regarding density?

**INTER** - A prefix occurring in loanwords from Latin, where it meant "between", "among"

- Inter-Operator variability suggests that a density reading by various MDs will vary depending on many factors

  *Recent study demonstrated only 61% agreement between MDs*

**INTRA** - A prefix meaning "within" used in the formation of compound words

- Intra-Operator variability suggests that a density reading by the same MD may vary depending on when the mammogram was read

  *Recent study demonstrated 20% variability*

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**Effect of Image Processing on Density**

- Hologic '05
- Siemens
- GE '07
- GE '08
- GE '09
- Hologic '10
- Hologic '11
- Hologic '12

**Current: Area-based Methods for Density Measurement**

- Use projected area of the dense tissue as relative estimates of the volumes

- These methods generate a breast density in the range of 0-100%

- ACR BIRADS density categories are assigned in quartiles of 25% (BIRADS 1-4)

- Circa 1976 – still in practice today

- Very Subjective

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**Effect of Image Processing on Density – Raw vs. Processed**

**Current: Area-based Methods for Density Measurement**

- Area: 0% 50% 50%
- Volumetric: 0% 12% 24%
VuCOMP, Inc.
- Dallas based company formed by three former employees of Texas Instruments
- First product was Mammography CAD
- Believes in area based density measurement
- Believes that density is defined as mass per unit volume, not volume per unit volume
- Believes that mammographic density is the bright areas in the mammogram that correspond to the regions of fibro glandular tissue

VuCOMP, Inc.
- Density category estimates calibrated to evaluations of expert radiologists,
- Thirteen radiologists read 1000 mammograms and provided their opinion on the density of breast.
- These were evaluated and a Bi-Rads like category was assigned to set a standard for the Vu-COMP product.

VuCOMP, Inc.
- Calculations are only done on the Cranial-caudal view
- VuCOMP, Inc. categories are not based on the ACR categories. They have based their categories on a much wider base than Volpara or Quantra (two companies based on volume based density measurement)
- Introduced the concept that the definition of breast density is the ratio of the volume of fibro glandular tissue to the total volume of the breast
**Secondary Capture**

**Density Measurement**

Quantra and Volpara

- is a software application used for volumetric breast density assessment.
- The software uses the “For Processing” images to calculate the amount of breast density.
- They use the four screening views for processing.
  - RCC, LCC, RMLO, LMLO
- Quantra is only approved for use on the Hologic system.

**Volume Based**

Density Measurement

“Whiteness” is not “Thickness”

- Uniform density masks any sense of thickness in a 2D mammography image
- Subcutaneous fat is not observed
- Thus accurate visual assessment is subjective and challenging

**Volumetric vs. Area Density**

- Fraction of fibroglandular tissue (pink) within a fatty breast:
  
  **By area:**
  \[
  \frac{4L \times 2L \times 0.2L}{4L \times 2L \times 2L} = \frac{100\%}{100\%} = 100\% \text{ vs. } 10\%
  \]

  **By volume:**
  \[
  \frac{4L \times 2L \times 0.2L}{4L \times 2L \times 2L} = \frac{100\%}{100\%} = 100\% \text{ vs. } 10\%
  \]
Quantra
- Analyzes each 2D image within a study
- Measures volume of the breast in cubic centimeters
- Measures volume of fibroglandular tissue in cubic centimeters
- Volumetric percentage of fibroglandular tissue (volume of fibroglandular tissue divided by volume of the breast)
- BI-RADS®-like score
- Area of breast density in percentage of total breast area, to facilitate study comparison
- Secondary Capture

Volpara Validation – FDA Approval for BI-RADS

The following process takes place by eye or by some early density assessment programs:

1. Decide how big the projected breast area is (orange line) and count the number of Breast Area Pixels.
2. For each pixel, now decide if the breast tissue between that pixel and the x-ray source is 100% fatty tissue, or 100% dense tissue. It is not continuous shades of grey.
3. Count up the Number of Dense Pixels.
4. Area Density = Number of Dense Pixels / Breast Area Pixels

Key difference, at each pixel:
- Area assessment says either 0 or 100% dense tissue between that pixel and the x-ray source.
- Volumetric assessment gives a continuous range between 0-100%.

With Area, effectively you do a volumetric assessment by eye then threshold it to say “this is dense tissue”, that thresholding does not occur with volumetric.

Note: A and B contribute the same to the overall area density score as they both represent “dense tissue”, but in the volumetric world A contributes more than B as it is denser tissue and this is why volumetric is the key to describing focal density properly.

www.volparadensity.com
Volume-based Methods for Density Measurement

Each pixel is analyzed and a pixel that is 100% fat is identified then serves as the "Baseline" from which every other pixel is compared.

Volumetric Breast Density = \frac{\text{Volume of Fibroglandular}}{\text{Volume of Breast Tissue}} (cm³)

- Utilizes volumetric measurement of the dense tissue and the volume of the breast.
- These methods typically generate a breast density in the range of 0 - 35%.
- Reflects the true physical density of the breast.
- Presents fibroglandular tissue, breast tissue, breast density, breast density grade.
- Quantitative.

Volpara™ VDG™ / BI-RADS® Category 1

Volpara™ VDG™ / BI-RADS® Category 2

Volpara can tell you the mass contains 63cm³ of dense tissue!!

The mass has contributed 20cm³ to the dense tissue volume.

Volpara Density Map

Volume-based Methods for Density Measurement

Volpara Density Map

Volumetric density of this breast is a high C because of the sheer volume of dense tissue present in the mass, area-wise it is a b.

Volpara can tell you the mass contains 63cm³ of dense tissue!!

Volpara™ Density Map

Volpara VDG™ / BI-RADS® Category 2

Completed before bi-rads changed

Volpara VDG™ / BI-RADS® Category 1

4.0% Density

Volpara™ Density Map

Completed before bi-rads changed
Volume-based Methods for Density Measurement

Volpara has more applications

- Analytics
  - Number of images
  - Tracks all imaging parameters of each patient
  - Tracks volumetric density per unit per RT
  - Provides data on each facility regarding patient population for comparison purposes

- Dose Tracking

Volpara

- Secondary Capture
- Structured Report

Volumetric Breast Density – The Actual Maths

\[ P(x,y) = \alpha D(x,y) + \beta \]

\[ D(x,y) = D_{\text{avg}} \frac{b \log \mathcal{E}_{\text{avg}}(x,y)}{\log \mathcal{E}_{\text{avg}}(x,y) + \sigma^2} \]

\[ \mathcal{E}_{\text{avg}}(x,y) = \int_{\mathbb{R}^2} \frac{1}{V_{\text{avg}}(x,y)} \mathcal{E}(x,y) \mathcal{H}(x,y) \mathcal{G}(\mathcal{H}(x,y)) e^{-\mu_{\text{avg}}(x,y) \xi} \, d\xi \]

\[ h\mu(\xi) = h_{\text{avg}}(x,y) \mu_{\text{avg}}(\xi) + h_{\text{fatt}}(x,y) \mu_{\text{fatt}}(\xi) \]

\[ h\mu(\xi) = h_{\text{avg}}(x,y) (\mu_{\text{avg}}(\xi) - \mu_{\text{fatt}}(\xi)) + H\mu_{\text{fatt}}(\xi) \]

Case Study: 2013 mammogram

- 66 year old woman
- Mamographic breast density (assessed visually by a radiologist) reported as ‘fatty <25% with residual glandular stroma.’
- Radiologist found no evidence of cancer and reported a ‘BI-RADS 2, benign finding.’
- Radiologist noted no significant change compared with prior studies dating back to 2009.
- Routine one-year follow-up recommended.

2014 mammogram + VolparaDensity

- Breast density reported as heterogeneously dense.
- Radiologist notes no dominant masses, areas of architectural distortion, or suspicious clusters of microcalcifications, and reports a BI-RADS 1 – negative finding.
- However, based on Volpara score, ultrasound ordered.
Supplementary screening breast ultrasound identified a 1.26 cm suspicious hypoechoic lesion at the 6 o’clock position, 1 cm from the nipple, in the right breast.

Ultrasound highly suggestive of malignancy (BI-RADS 5)

Woman recommended for surgical consultation and biopsy.

Surgical and pathological findings identified a 1.7 cm, high grade (Grade 3), triple-negative (estrogen and progesterone receptor negative and Her-2/neu negative) invasive ductal carcinoma.

Case courtesy of Jean Weigert, MD, FACR
The Hospital of Central Connecticut

Each vendor has taken a different approach to the design of their tomosynthesis system.

Hologic acquires 15 projections over a 15° scan angle.

GE acquires 9 projections over a 24° scan angle.

Siemens acquires 25 projections over a 50° scan angle.

However, for all three techniques, each of the acquired tomosynthesis projections is simply a low dose, 2D projection mammogram.

For each manufacturer, the VolparaDensity algorithm works on the acquired projections from the raw tomosynthesis data sets in the same way as it processes the raw data of a conventional 2D mammogram (details beyond this are proprietary).
Photon Counting

- Studies have shown that accurate measurement of breast density can be achieved via dual energy imaging.
- Uses a standard mammogram as a low energy image and then acquires an additional high energy image.
- By measuring the dual energy of adipose and fibroglandular tissues, accurate measurements of both density and thickness can be obtained.
- However, the additional, high energy image increases mean glandular dose.

Spectral Imaging

- Photon counting detector
- Sorts photons into high or low energy categories which eliminates the need for two exposures.
- Rather than estimating density, Spectral Imaging differentiates between adipose and fibroglandular tissue.
- It actually measures the volumetric breast density.

Spectral Breast Density Measurement Tool

- Optional feature on Philips MicroDose Mammography system
- Density data is sent along with the MicroDose images directly to the review station
- Data is transferred as a Structured Report
- MicroDose Density Score (Correlated to BI-RADS® breast density score)

The End