CO-RELATING MAMMOGRAPHIC DENSITY, BREAST CANCER RISK AND A FULLY AUTOMATED VOLUMETRIC DENSITY MEASUREMENT (VOLPARA™)

Bushra Wasim, Khalid M. Khan, Ariane Chan, Kamran Hameed, Farah Habib

1 Department of Anatomy, Ziauddin University, Karachi, Pakistan.
2 Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait.
3 Global Medical Affairs, Volpara Solutions Limited
4 Department of Rheumatology, Ziauddin University, Karachi, Pakistan.
5 Research Associate, Patel Hospital, Karachi, Pakistan.

ABSTRACT

Breast cancer and mammographic density have been directly related i.e. the greater the breast density the greater is the risk of developing breast cancer. Accuracy of reading mammograms is reader subjective. The Gold standard is Cumulus which is quantitative but still reader subjective. In the recent past more stress is on developing fully automated methods and volumetric assessment of mammographic densities which are more objective and quantitative. In this review a quick glance is given to various methods and their strengths.

Key Words: Mammographic density, Volumetric assessment, Cumulus

Introduction

Breast Cancer is one of the most common cancers worldwide. In 2010, nearly 1.5 million women were diagnosed with breast cancer. The highest incidence rates are present in UK, US, Australia and New Zealand. Pakistani women have a lifetime risk of 10% of developing breast cancer, i.e. every 1/9 females will develop breast cancer in their lifetime.1 Pakistan has a significant cancer burden and a rapid increase in breast cancer incidence has been observed in the last five years. The incidence rate and the rise in the Karachi south are comparable to the highest risk regions of the world.2 Over the last 20 years researchers have discovered links between breast composition (usually termed “breast density”) and breast cancer risk. In this review we explain about the breast density, how to measure it, and why it is important to us.

What is breast density and how is it measured. This important component is related to breast cancer and mammography. Radiographically, only two types of tissues are visible in the breast; parenchyma and stroma. Fibroglandular (or “dense”) tissue appears as white and includes the glandular as well as epithelial tissue. The stroma is predominantly fat and since it has lower x-ray attenuation coefficient, appears black or transparent on film screen mammogram. The degree of whiteness of an image is termed its Mammographic Density (MD).3 Women with high MD has an increased amount of fibroglandular tissue relative to fat. All around the world clinically a mammogram is read and scored via the BI-RADS (breast imaging reporting and data system) system from the American College of Radiology. With this system four categories of breast density have been identified which are as follows:4

1 Department of Anatomy, Ziauddin University, Karachi, Pakistan.
2 Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait.
3 Global Medical Affairs, Volpara Solutions Limited
4 Department of Rheumatology, Ziauddin University, Karachi, Pakistan.
5 Research Associate, Patel Hospital, Karachi, Pakistan.

Submitted 13 May 2015, Accepted 3 June 2015

Pakistani Journal of Radiology
Breast Density: BI-RADS type 1 Mostly fat (fibroglan-
dular tissue is 0-25% of the breast)

Breast Density: BI-RADS type 2 Scattered density
(fibroglanular tissue is 25-50% of the breast)

Breast Density: BI-RADS type 3 Heterogeneous
density (fibroglanular tissue is between 50-75% of
the breast)

Breast Density: BI-RADS type 4 extremely dense
(fibroglanular tissue is more than 75% of the breast).

There is now extensive evidence supporting the fact
that MD is an independent risk factor for breast
cancer. Women with higher MD i.e. more than 75%
have a 5-fold increased risk of breast cancer, compared
to women with the lowest amount of MD.

Methods of Measuring MD in
the past and present

Methods for MD measurement were subjective and
qualitative but fortunately newer methods have
recently been developed which are more objective
and quantitative. A review done in 2008 classified
MD measurement techniques into two groups:

1. Qualitative-Wolfe and BI-RADS
2. Quantitative-Cumulus (semi-automated thresh-
holding) volumetric density assessments.

Each of the above mentioned methods have their
own limitations. For example, the qualitative methods
are very subjective whereas the quantitative semi-
automated (Cumulus) is an accepted method, yet,
reader subjective. The fully automated method with
3D volumetric assessment of the breast tissue is a
more ideal method. In volumetric measurements, the
actual physical composition of the breast is deter-
mined and evidence is growing that it is a more
powerful breast cancer risk predictor than the qualita-
tive techniques and Cumulus. Cumulus was developed by Byng et al at Sunnybrook

Hospital in Toronto and Boyd reported that the 10%
of women with more than 75% increased breast
density had a 4-5 fold increased risk as compared
to women with no areas of increased breast density.
In all these methods, user defined threshold method
and the density calculation was area based. There
was subjectivity observed in these methods due to
inter and intra-observer variability, which can be
reduced with training.

Since Cumulus has been the Gold standard for breast
density measurement, a recent article, a comparison
was done between the volumetric breast density
method (Volpara™) and Cumulus. The reason for
this comparison was to highlight the interest in fully
automated volumetric measures of breast density
which eliminate the user variability, time factor and
most of all to interpret the breast as a 3D organ.
In their results the authors showed a strong relationship
between Volpara™ BD% and BI-RADS categories.
There was again a strong relationship between Vol-
para BD% and Cumulus and hence they concluded
that since Volpara™ correlates well with the Gold
standard measure of breast density it is expected
that there should be a strong relationship between
Volpara™ and breast cancer risk. There are differ-
ent methods of measuring volumetric density with
positive and negative points.

Computed Tomography: This method involves
reconstructing a three-dimensional x-ray attenuation
coefficient of tissues in a series of planar images.
Limitations of this method include the excessive
amount of radiation and high cost. Furthermore
because the patient is prone on the table some tissue
can be missed and therefore, the reconstruction is
adversely affected.

In Tomosynthesis the projection of images are at
different angles about the breast on a specialized
digital mammography system and these images are
reconstructed in quasi three-dimensional planer
images of the x-ray attenuation coefficient of
the breast tissue. Limitations of this method again include
high cost, requirement of trained personnel and insuf-
ficient data to take on this method for research pur-
poses.

Another method known as Dual Energy x-ray absorp-
tiometry involves transmission of rays through the
breast. Transmitted rays are analyzed in terms of
effective thickness of fibro glandular tissue and fat.
A limitation of this method is that an entirely different
procedure is required in addition to a mammogram which increases the cost.14

What Is Digital Mammography?
In digital mammography the screen-film image receptor is replaced by a detector that produces an electronic signal that precisely targets the x-rays from the breast over a wide area. This signal is digitized and stored in the computer. The greatest advantage of this technology is that the image can be reproduced, modified, enhanced and brightened for further evaluation. The amount of radiation used is less but patients with large breasts need additional exposure.3,13
In 2001 a study trial was conducted called the “Digital Mammographic Imaging Screening Trial (DMIST), conducted by the American College of Radiology (ARC) Imaging network. They defined three categories:

1. under age 50
2. of any age with heterogeneous or extremely dense breast
3. Pre or Perimenopausal women of any age (defined as women who had a last menstrual period within 12 months of their mammograms.15

A n important point to consider is that there are two basic types of digital mammography images produced, one is known as “For Processing” or “Raw image” and the other is “For Presentation” or “Processed image”. The raw image is derived from the detector signal coming from the breast and is closely related to the breast composition. These images undergo extensive processing for display on a computer screen. It is recommended that density analysis from digital mammograms should be performed using the raw data image. To keep the inter-and intra-observer subjectivity to a minimum and in this regard the choice which is available is fully automated software Volpara™ which measures fibroglandular tissue in 3D and gives a full volumetric density which is percentage of the fibroglandular tissue. It is a real physical measure and the formula being used is:

\[
\text{Volumetric Breast Density} = 100 \times \frac{\text{volume of fibroglandular tissue (cm}^3\text{)}}{\text{volume of breast tissue cm}^3}\]

To align with the current clinical system and to facilitate the understanding of the radiologists, mapping to the BI-RADS density categories is essential:

- 0% - 4.5% = BI-RADS - 1
- 4.5% - 7.5% = BI-RADS - 2
- 7.5% - 15.5% = BI-RADS - 3
- > 15.5% = BI-RADS - 4

These percentages are different to the ones stated earlier because these are volumetric compared to area ones.

Digital Mammography
Concept of using x-ray to visualize breast tissue was first put forth by Dr Albert Salomon, a German surgeon in 1913.
In 1950’s Jacob Gershon began to advocate widespread use of x-rays for screening purpose. In December 2005 RSNA brings digital mammography to USA.
In this process low energy x-rays (30 KV) are used on a digital model machine with an x-ray tube comprising a Molybdenum anode and Molybdenum filter. During the image acquisition process the breast is compressed. Parallel plate compression even out the thickness of breast tissue to increase image quality when the x-rays pass through it, and reduce both the amount of scattered radiation and required radiation dose. Additionally holding the breast still helps to prevent motion blur. Two standard views are taken i.e. craniocaudal view and Mediolateral oblique.

Discussion
It has now been established that MD is a risk factor for breast cancer and that the disease starts early in life, prior to the age at which mammography is recommended. A lot of discussion is on whether women in their 40’s should have annual or bi-annual mammograms. According to Web Med16 Breast cancer risk in younger women is higher than previously thought and so is the recurrence rate.
In a recent article a comparison was made between Cumulus and the new volumetric breast density method. Volpara™, volumetric breast density designed to be run on Full Field Digital Mammographic images and was compared to breast density as assessed from area-based visual technique, the standard BI-RADS technique as well as semi-automated tech-
The authors concluded that Volpara™ correlates well with the Gold standard measure of breast density (Cumulus) and they expect to find a strong relationship between the Volpara™ and breast cancer risk. However, the intention is to promote earlier mammograms in all females who have a family history rather than wait for the recommended age for mammography. Most important factor is to obtain a volumetric assessment of breast density through a fully automated method in young females and correlate breast density to breast cancer risk.

Conflict of Interest: Mr Ariane is an employee of Volpara.

References

4. B.Halls S. Breast Density classifications according to the BI-RADS lexicon. 2010.