REVIEW ARTICLE

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

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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 life time 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.

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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]

Breast Density: BI-RADS type 1 Mostly fat (fibroglandular tissue is 0-25% of the breast)

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

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

Breast Density: BI-RADS type 4 extremely dense (fibroglandular 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.[5] Women with higher MD i.e. more than 75% have a 5-fold increased risk of breast cancer,[6,7] 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.[3] A review done in 2008 classified MD measurement techniques into two groups:

1.Qualitative-Wolfe and BI-RADS
2.Quantitative-Cumulus (semi-automated thresholding) 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 determined and evidence is growing that it is a more powerful breast cancer risk predictor than the qualitative techniques and Cumulus.[8]
Cumulus was developed by Byng et al[9] 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.[10] There was subjectivity observed in these methods due to inter and intra-observer variability, which can be reduced with training.[11,12]
Since Cumulus has been the Gold standard for breast density measurement, ina 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 Volpara 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.[13] There are different 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 co-efficient of the breast tissue. Limitations of this method again include high cost, requirement of trained personnel and insufficient data to take on this method for research purposes.
Another method known as Dual Energy x-ray absorptiometry 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]

An 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 mea-sure and the formula being used is:

Volumetric Breast Density= 100 x volume of fibroglandular tissue (cm3)/volume of breast tissue cm³)

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 evens 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 Med[16] Breast cancer risk in younger women is higher than pre-viously 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-

nique Cumulus. 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.

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