Development of a Quantitative Estimation of Mammographically Breast Density

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ABSTRACT

Objective: **Increased mammographic breast density is a moderate independent risk factor for breast cancer. Assessment of breast density may become useful in risk assessment and prevention decisions. To evaluate the association between mammographic density and breast cancer risk, a simple observer-assisted technique called interactive thresholding was developed.**

Methods: **For providing, a quantitative estimation of mammographically dense tissue, in this study computer assisted measurements were carried out using Adobe AIR software. For thresholding technique, software named 'X-ray Image Analyzer' was programmed in Adobe AIR language version - Action script 3.0. runtime version- Flash player 9, AIR 1.0, and flash Lite-4. Interactive thresholding technique was applied to digitized film screen mammograms, which assesses the proportion of radio graphically dense tissue in the mammographic image representing mammographic density. The technique evaluated for 36 mammograms of 18 women who underwent referral mammography in a hospital at Dhaka city from October 2010 to October 2011.**

Results: **The women in the selected group were in age range of 20 to 60 years, with a mean age of 44±9 and median age is 45 yrs. The technique was found to be very reliable with an intra-class correlation coefficient between observers typically R = 0.887. This technique may have a role in routine mammographic analysis for the purpose of assessing risk categories and as a tool in studies of the etiology of breast cancer, in particular for monitoring changes in breast parenchyma during potential preventive interventions.**

Conclusion: **It is possible to use the interactive segmentation technique for other projections of the breast, such as the medio-lateral oblique view. In this case, however, it is necessary to perform a manual segmentation to remove the image of the pectoral muscle from the analysis. This technique can be employ as a tool in many clinical studies.**

Keywords: **Mammographic breast density, Quantitative estimation, Breast cancer**

INTRODUCTION

Variation in the radiographic appearance of the breast reflects differences in tissue composition (1). Fibro-glandular tissue consisting of the functional elements or parenchyma in the breast attenuates x-rays to a greater degree than fat, causing areas composed of significant amounts of the Fibro-glandular tissue to appear bright on a film mammogram (2). The proportion of the lighter or dense regions on the mammogram, characterized as 'mammographic density'. When quantifying mammographic density it would be desirable to estimate the proportion of dense tissue in the breast.

Radiologist and medical physicists are two groups of medical professionals who routinely use mammographic breast density in their profession. The radiologist estimates breast tissue density qualitatively to determine the probability of detecting a cancer or other breast abnormalities from the mammogram. The parenchyma patterns in a mammogram have been associated with an increased risk of breast cancer by population studies that have correlated cancer incidence with breast density (3). The medical physicist estimates breast density quantitatively to determine average glandular dose (MGD) using a dose conversion factor that correlates the breast entrance skin exposure to glandular tissue dose. Over the years, both groups of professionals have attempted to expedite the process of estimating breast density. The only accurate method to quantify glandular tissue content in a breast is by biopsy. Biopsy ensures a quantifiable measure, but it is not practical, and a small tissues sample is not representative of the whole breast. Mammography

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images are highly dependent on the compressed thickness of the breast during the mammographic examination and on the spectrum of the x-ray beam (4). It is, therefore, difficult to evaluate volume of dense tissue, especially in retrospective analysis of mammograms or in studies where images acquired at a number of different facilities.

Initial methods for assessing mammographic density as well as glandular tissue distribution were entirely subjective and qualitative; however, in the past few years methods have been developed to provide more objective and quantitative density measurements. Attempts to develop a reproducible quantitative method of assessing breast density began in the early 1980s (5). Visual estimation of the percentage of the breast occupied by breast tissue has been used frequently. In the United States, the Breast Imaging Reporting and Data System (BI-RADS) was developed to standardize mammography reporting terminology and recommendation categories (6). BI-RADS density classification is included in the report to inform referring physicians of the decline in sensitivity of mammography with increasing breast density. It was not intended to serve as a method of measuring breast density.

The ability to identify women at greater risk from breast cancer has application in etiologic studies of the disease. This may include potential preventive interventions, for which the ability to monitor changes in mammographic density would be of interest (7). As a better reflection of continuous variations in density within the breast, it is the goal of this work to develop a more quantitative scale for the analysis of mammographic densities. We describe an approach for quantitative analysis of mammographic parenchyma based on the interactive segmentation of digitized film mammograms trained image interpreter. Segmentation is accomplished with a thresholding technique, which outlines regions of similar image brightness and thereby provides a simple decision criterion for mammographic density, which is applied uniformly across the image. Quantification is then performed automatically by counting pixels within the regions identified as representative of radiographically dense tissue.

METHOD

2.1. Selection of images

Cases in this study were selected from referral patient in a risk assessment study made from October 2010 to October 2011. The women in the selected cohort were in age range from 20 to 60 years, with a mean age of 44. As part of that study, each woman had two mammogram of cranial-caudal view (CC), performed with modern mammographic units, high-contrast mammographic film, and dedicated extended processing. In addition, a regular quality control programme was in effect. One of the authors experienced in the classification of mammographic parenchyma, classified both cranial-caudal image from 18 women. From the eighteen selected cases, both the right and left cranial-caudal projections a total 36 images were considered in these experiments.

2.2. Digitization and Display

The images were digitized using a Fuji FCR XG5000 (model: CR-IR 362) laser film scanner (Fuji Corporation, Tokyo). The scanner provides a12-bits (4096-grey-level) output, which is linear in the range of 0 - 4.0 optical densities. As a trade-off between resolution and image size, films were digitized with 10 pixels/mm. The format of 1770 x 2370 pixels, covering an area of 180 mm x 240 mm, was used to accommodate the range of projected breast areas encountered in these images, which were averaged to 1770 x 2370 pixels for analysis. For the display purposes, the images were converted to 256 grey levels by means of a linear transformation.

2.3 Density Analysis

For providing a quantitative estimate of mammographically dense tissue, computer assisted measurements were carried out using Adobe AIR software. In this study for interactive threshold technique software named 'X-ray Image Analyzer' was programmed in Adobe AIR language version –Action script 3.0 runtime

version- Flash player 9, AIR 1.0, and flash Lite-4. In this programme the Bitmap data class works with pixel of digitized image. It was used to create arbitrary sized transparent and opaque Bitmap images to manipulate them in various ways at runtime.

A Bitmap data object contains an array of pixel data. These data can represent either a fully opaque Bitmap or a transparent Bitmap that contains alpha channel data. Either type of Bitmap data object is stored as a buffer of 32-bit integers. Each 32-bit integer determines the properties of a single pixel in the bitmap.

Each 32-bit integer is a combination of four 8-bit channel values (from 0 to 255) that describe the alpha transparency and the red, green, and blue (ARGB) values of the pixel. For ARGB values, the most significant byte represents the alpha channel value, followed by red, green, and blue colours.

Measurement with a sample image with the thresholding technique is illustrated in Figure 1. In the digitized image, pixels have a grey-level value i, that ranges between zero (an essentially opaque film) and i_{max} (a clear film), where i_{max} is the maximum value provided by the digitizer (i_{max} = 4096). The computer display is equipped with a colour, graphics overlay, with which an observer can interactively highlight a selected pixel value in colour, by manipulation of a trackball.

Interface labeling of the image for analysis is given in Figure 1. The input value of the programme measurement is shown by the blank box represented by input, where the meaning of the terms is also given.

Estimated output results from the programme are obtained as explained in Figure 1. Here A and B represent two output results calculated from the program. It gives histogram of glandular tissue, area of the breast and area of the glandular tissue. For the measurements an observer begins by selecting a grey value, i_{edge}, which acts as a threshold to separate the image of the breast from the background. An edge detection algorithm

surveys the image along lines from the chest wall toward the nipple until pixel values fall below the edge threshold, thereby identifying the pixels lying within the projection of the breast image. The green line in Figure 2 shows the edge of the breast. We define x_i as the number of pixels at grey level i, and calculate the histogram of pixel values within the boundary of the breast.
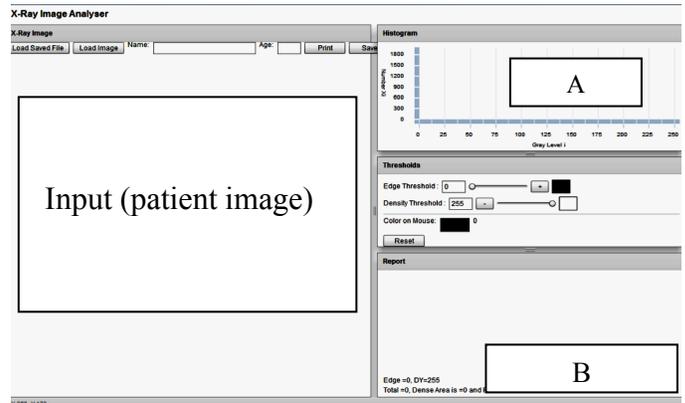
Figure. 1 Interface for quantitative estimation of mammography density

The summation over the histogram is representative of the size of the projected area of the breast in the image:

$$A = \sum_{i=i_{edge}}^{i_{max}} x_i \ldots\ldots\ldots\ldots\ldots 1$$

A second threshold, i_{DY}, then selected to identify the edges of regions representative of radiographically dense tissue in the image and shown by the blue bright line in Figure 3.

Pixels in the regions identified as dense parenchyma have a grey value above i_{DY}. The proportion of radiographic density is calculated as the percentage, PD, of the entire projected area of the breast, A, consisting of 'dense' pixels, i.e.

$$PD = \frac{\sum_{i=i_{DY}}^{i_{max}} x_i}{A} \times 100\% \ldots\ldots\ldots 2$$

A tool is provided to allow exclusion of the area of the image of the pectorals muscle (if it appears on the mammogram) from the calculation.

Because of variations in image acquisition (e.g., kilovoltage and breast compression) and processing

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techniques (e.g. film development time and temperature), the thresholds i_{edge} and i_{DY} were determined specifically for each patient image being evaluated. Comparisons between images were made based on the measured A and PD rather than on the thresholds directly.
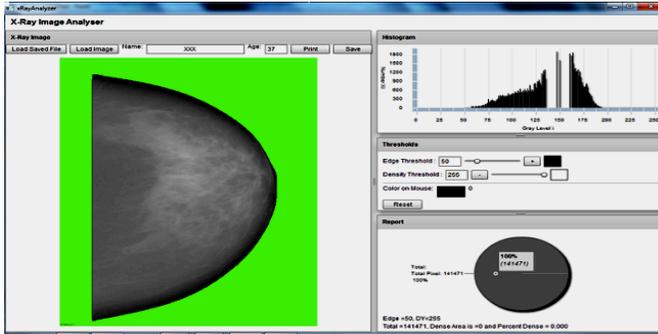
Figure 2: The digitized mammogram is displayed on the computer screen and a threshold i_{edge} selected by the operator to segment the breast from the surrounding background (green Area).

2.4. Observer

Two observer viewed the images at the workstation and interactively determined thresholds, i_{edge} and i_{DY}, to assess PD for images in this study. Each reader evaluated all images at a single session. Readers were unrestricted in their viewing times but typically took about 2 minute to evaluate each image.
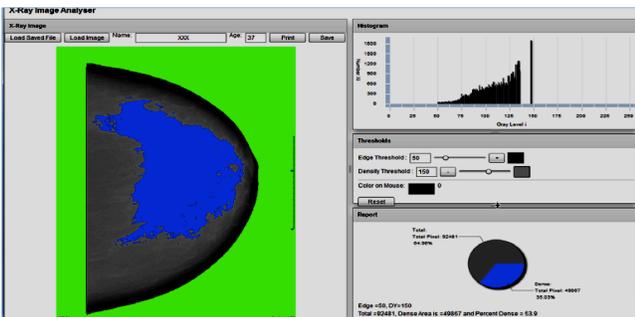
Figure 3: Threshold i_{DY} is set to identify the regions of density. The algorithm indicates these pixels by blue overlay.
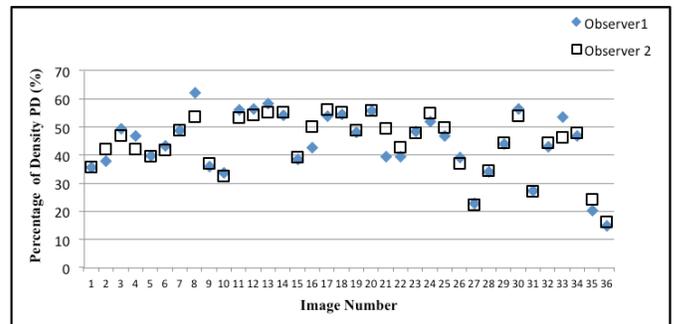
2.4. Reliability

The reliability of the measurements of PD and breast area, A, were evaluated in terms of both the intra-observer and inter-observer variability. Both observer read 36 images and 10 repeat images interspersed in a single reading session (46 images

in all). Inter-observer variability was determined by comparing reader's estimation of PD and breast area A for the set of 36 images. Assessment of Intra-observer variability was done by comparing the first and second readings of the 10 repeated images.

In both cases, an 'intraclass correlation coefficient' was used as a summary statistic of reproducibility or reliability. The Intra-Class Correlation Coefficient (ICC) typically used when we have a number of different interviewers, observers or assessors within our survey. In most cases the value of the ICC ranges from 0 to 1, whereas the ICC approaches a value of one then we see a perfect agreement between observers and as the ICC approaches a value of zero then we see no agreement between observers. Here we have calculated ICC using Karl Pearson's formula. To calculate this coefficient, an analysis of variance **(ANOVA)** performed to break down the total variance into components due to cases, observers, and error.

RESULT AND DISCUSSION

Figure 4: Distribution of PD for two observers.

The reliability of readers in estimation of PD from the interactively specified thresholds i_{edge} and i_{DY} was made. The intra-class correlation between the two observers was measured at R = 0.887. This agreement is considerably higher than that reported elsewhere. For example, in an earlier study by Boyd et al (5). The high level of agreement here may be explained by the fact that the observers had extensive experience in the classification of mammographic parenchyma and were co-operatively trained in the classification of radiographic density before performing their independent classifications in this study.

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To assess the variability in determination of PD, standard deviations, both within and between observers, were calculated. The within-observer standard deviation was calculated for each observer as the deviation about the mean of two readings over the 10 repeated cases in the reading group. The mean value of σ_{within} over two readers was 2.41. The between-observer variation was calculated as the deviation from the mean PD (over all two observers' measurements) for the 36 images read in this study. Overall a $\sigma_{between} = 5.939$ was calculated. Considering the measurement of PD for a single image by a member of the reader panel, we estimate, based on the combination of intra-observer and inter-observer error, an effective standard deviation $[(\sigma_{within})^2 + (\sigma_{between})^2]^{1/2}$ of 6.409 in units of PD.

The thresholding technique also permits an assessment of the total projected area of the breast through the number of pixels in the image within the i_{edge} threshold as described in equation (1). In addition to PD, this variable is of interest when studying changes in mammographic patterns in longitudinal studies. Almost perfect agreement (intra-class correlation, R > 0.98) was observed both within and between observers for measurements of the projected area of the breast. Such good agreement was anticipated because the identification of the breast from the background in the image (i.e. the selection of the threshold, i_{edge}, which outlines the edge of the breast) is a very easy task. In general, the i_{edge} threshold lies in a region of the histogram that is flat and of low frequency. Slight variations in the selection of this threshold will therefore not greatly affect the determination of A (projected area of breast). Within - and between-observer variability for 'A' (projected area of breast) was determined in a manner analogous to that for PD. We found that the mean value of σ_{within} was 325.97 pixels and that of $\sigma_{between}$ was 2693.37 pixels. Based on a combination of between- and within-observer variation we estimate an effective standard deviation of 2713 pixels in the determination of A. The size of the breast ranged from 66010 to 141500 pixels.

CONCLUSION

The interactive thresholding approach facilitates the quantification of mammographic density and results in good agreement both within and between observers. The variability, by the standard deviations of PD, is dominated by between-reader differences. This motivates the development of estimation that are truly objective and, therefore, both observer independent and reproducible. Ideally, such a method would be automatic, removing the need for highly trained personnel to evaluate mammographic parenchyma. Dependent on the magnitude of the risk identified, risk prediction by parenchymal classifications may be important in screening programmes, particularly in identifying optimum intervals for screening based on risk (8). More importantly, a continuous-scale quantitative classification is well suited to monitoring potential preventive interventions (7), which may give rise to changes in mammographic parenchyma.

It is possible to use the interactive segmentation technique for other projections of the breast, such as the medio-lateral oblique view. However, it would then be necessary to perform a manual segmentation to remove the image of the pectoral muscle from the analysis. This technique may be employ as a tool in many clinical studies.

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