Digital Mammography

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Volumetric Breast Density and Breast Cancer Risk Factors in a Screening Population

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Abstract. Breast density is positively linked to the risk of developing breast cancer. Furthermore, the addition of breast density as an input to breast cancer risk prediction models has been shown to improve their predictive power. Such models are used in the management of women at high risk but could potentially be used to determine screening strategy. A stepwedge-based technique has been used to measure volumetric density from the mammograms of 1,289 women in the UK screening programme who additionally completed a questionnaire on risk-related factors. The sample had a mean age of 60.1 (range 48.0 – 78.0), a mean breast thickness of 59mm (range 21 – 102mm) and a mean volumetric breast density of 11% (range 0.5 – 58%). Using Pearson's correlation coefficient, breast density was found to be significantly correlated with weight (r = -0.45), body mass index (r = -0.48), age (r = -0.13) and breast thickness (r =-0.65) at the p = 0.01 level. Absolute glandular volume was also found to be significantly correlated with these parameters although the extent of correlation was weaker.

Keywords: breast density, volumetric technique, risk factors.

1 Introduction

The amount of dense (non-fatty) tissue within the breast is strongly linked to the risk of developing breast cancer [1 – 3]. A number of techniques exist for the measurement of breast density, either by area [3 – 6] or volume [7 – 11]. Although area-based techniques have shown strong correlations between breast density and risk [1 – 3], results are generally based on an interpretation of the mammogram which equates brightness of the image with density; the validity of this assumption has, however, been questioned [12]. Volumetric methods seek to provide a quantitative and more objective approach which takes into account the true three-dimensional nature of the breast and its component tissues.

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2 Materials and Methods

6,000 women attending routine breast screening were invited to participate in a feasibility study which aimed to provide descriptive statistics on breast density distribution in the screening population and to examine the relationship of volumetric breast density to other breast cancer risk factors, collected via questionnaire. The inclusion of breast density in risk prediction models has been shown to offer improved accuracy in the identification of women at high risk of developing breast cancer [13]. Questionnaire data included age at examination, height, weight (and hence body mass index, BMI), date of first pregnancy, ages of menarche and menopause, ethnicity and family history of breast cancer (mother or sister only) including the age at which breast cancer was diagnosed in this relative. Information regarding previous breast disease and use of hormone replacement therapy (HRT) was available in the patients' notes.

Mammograms were taken as usual. A stepwedge calibrated against glandular and adipose tissue equivalent material was placed on the breast support platform and radio-opaque magnification markers were placed on the compression paddle, to facilitate accurate determination of breast thickness across the mammogram [14]. The images were anonymised and digitised and a semi-automated method was used to assess breast density [11]. An operator was prompted to select the radio-opaque markers and define two steps on the stepwedge. An approximate location for the breast edge was determined by i) applying a global threshold based on analysis of the grey-level histogram in each mammogram ii) applying morphological operators to the resulting binary image to isolate the main breast region. The approximate breast edge location was used to initialise an adaptation of active contour algorithm which then computed a more precise (and locally smooth) demarcation of the breast edge. A thickness of glandular tissue was determined at each pixel, allowing breast density to be expressed in terms of the absolute glandular volume and the percentage breast density (defined as glandular volume / total breast volume). An example of the resulting glandular thickness map is shown in Figure 1.

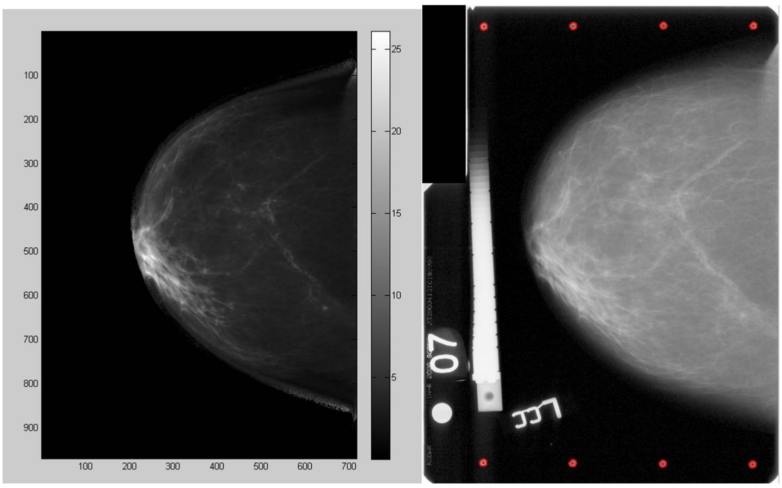

Fig. 1. Glandular thickness map shown alongside an original mammogram

The absolute glandular volume and percentage breast density were calculated for each view. The differences between breast density in the left / right and cranio-caudal (CC) / medio-lateral oblique (MLO) views were examined using paired t-tests. Correlations between breast density and a number of risk-related parameters have been assessed using Pearson's correlation co-efficient.

Results have been compared to those from previous work, which examined the correlation of these parameters with radiologist-assessed percentage breast density for a subset of 294 women from this sample [15].

3 Results

3.1 Population Demographics

1,289 women consented to take part in the study and had their breast density calculated using the method described above. The demographics of the population sample are shown in Table 1. The values quoted for breast thickness, glandular volume and breast density are the average of all four views. The maximum measure of breast thickness is used (i.e. that measured at the chest wall).

Table 1. Demographics of the population sample

Parameter	**Mean**	**Minimum**	**Maximum**	**Standard deviation**
Age (years)	60.1	48.0	78.0	5.7
Weight (kg)	69.7	32.3	178.1	13.8
Body Mass Index (kgm^{-2})	26.9	13.8	74.1	5.2
Breast thickness (mm)	58.9	20.9	102.3	12.1
Glandular volume (cm^3)	72	8	626	49
Breast density: mean of four views (%)	11.0	0.5	58.0	8.8

3.2 Variation in Breast Density by View

The variation in breast density by view was assessed using paired t-tests. The results are shown in Table 2. Glandular volume and breast density were found to vary with mammographic view. The difference between left and right breasts was not significant but interestingly, the difference between the CC and the MLO view was significant.

Table 2. Variation in volumetric breast density by view

	Mean difference	95% Confidence Interval		Significant difference	p-value
		Lower	Upper		
LMLO – LCC	-1.70	-1.89	-1.50	Yes	<0.01
RMLO – RCC	-1.39	-1.59	-1.20	Yes	<0.01
RCC – LCC	-0.02	-0.21	0.17	No	0.41
RMLO – LMLO	-0.01	-0.19	0.18	No	0.47

3.3 Correlation of Breast Density with Other Risk-Related Factors

The correlations of breast density with age and BMI are shown in Figures 2 and 3 respectively. The correlation of absolute glandular volume and percentage breast density with these and other parameters is compared in Table 3. All correlations were significant at the p=0.01 level.

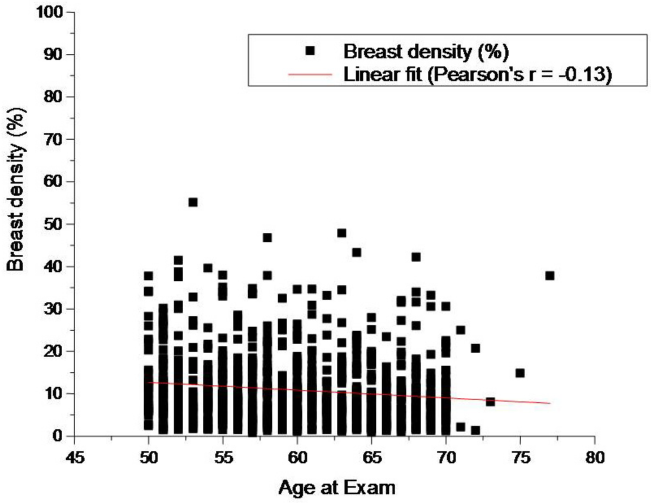

Fig. 2. Breast density versus age at examination

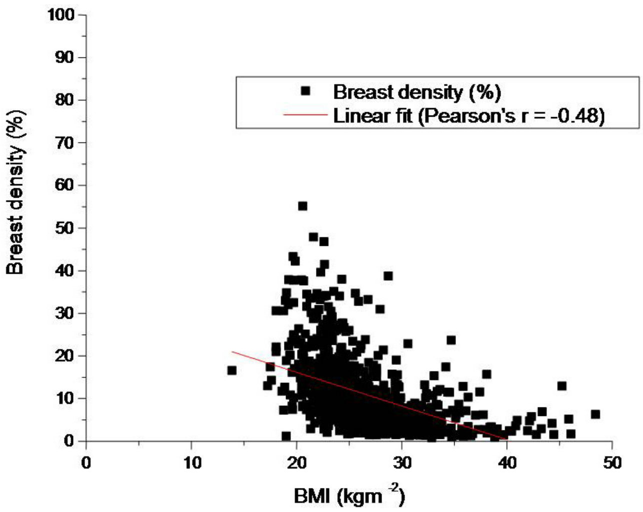

Fig. 3. Breast density versus body mass index (BMI)

As expected, breast density was found to decrease with age, weight, BMI and breast thickness. Glandular volume also decreased with these parameters although the strength of correlation was weaker. The stronger association with percent density can be explained by the evidence that breast volumes increase with weight but there is not a large change in gland volume. The association with BMI for both density variables reflected the association and strength of association with weight.

3.4 Comparison with Radiologist Visual Assessment

294 women from this sample had their breast density measured by a radiologist using a visual analogue scale. The mean age of this sample was 60.2 (range 50 – 72) and the mean weight was 69.3kg (range 41.3 – 139.9kg). Within this sample, the mean breast density was 27% (range 2 – 88%). It is interesting to note that the CC view was denser than the MLO view by an average of 0.5% (left) and 0.8% (right), a trend that agrees with the results in Table 2 for volumetric breast density. However, the right breast density was found to be greater than the left breast density by an average of 1.1%; no significant difference was observed between left and right when using the volumetric method.

The correlations between visually-assessed breast density with risk-related factors are shown in Table 3. Although the trends are similar to those for volumetric breast density, the strength of correlation is generally weaker for visually-assessed density. The relationship with BMI was significant at the p=0.01 level; the relationship with weight was significant at the p=0.05 level.

Table 3. Correlation of glandular volume and breast density with risk-related factors

	Pearson's correlation co-efficient (r)		
	Glandular volume (cm^3)	Volumetric Breast density (%)	Visually-Assessed Breast density (%)
Breast thickness (mm)	-0.11	-0.65	-0.30
Age (years)	-0.18	-0.13	-0.18
Weight (kg)	-0.11	-0.45	-0.29
BMI (kgm^{-2})	-0.16	-0.48	-0.41

4 Conclusion

All women taking part in the study had their breast density measured for each mammographic view using a semi-automated volumetric method. The average breast density of the sample was 11% (range 0.5 – 58%). As expected, breast density was found to decrease as breast thickness increased (r = -0.65). There were also strong negative correlations (p = 0.01) with weight (r = -0.45) and BMI (r = -0.48). Significant correlations were also observed between these parameters and absolute glandular volume although the strength of the correlation was lower. This was expected as although breast volume increases with weight, weight gain is associated with an increase in adipose, rather than glandular tissue.

Our previous work examined the relationship between visually-assessed breast density and risk-related factors. The mean breast density using this method was found to be higher than the software-based measure of volumetric breast density. The visual method was only applied to a subset of the women taking part in the study but the mean age and weight were similar for both samples, as were the ranges for these parameters. Other studies comparing area-based and volumetric techniques have shown that the measure of breast density is higher using area-based techniques [16, 17]. It is interesting to note that the strength of association between visually-assessed density with weight, BMI and breast thickness was lower than that for volumetric density.

Glandular volume and volumetric breast density were found to vary with mammographic view. The difference between left and right breasts was not significant but the difference between the CC and the MLO view was significant. On average, the CC view was found to be denser than the MLO view, a result also supported by radiologist visual-assessment. This suggests that it may not be adequate to measure density for one view only. There is evidence to suggest that the strength of the association between breast density and risk increases when considering both the CC and MLO views compared to the MLO view only [18]. However, this paper was based on a study using radiologist visual assessment of density and other studies using automated techniques have shown that it is possible to use one view only [19].

This study examined the relationship between volumetric breast density and other risk factors for breast cancer. Ideally, we would have liked to examine the relationship with breast cancer risk itself. Independent t-tests were used to compare women who had previously had breast cancer with those who had not. Unfortunately, the analysis into this variable was hampered by the small sample size and the difficulty in accurately matching controls. Meaningful comparison was therefore impossible. Our semi-automated volumetric method is currently being used in a large-scale multidisciplinary study which aims to develop risk-prediction models for the screening population. A number of different methods are being applied and their relationship with risk will be compared. Work is underway to adapt our method to make it suitable for full-field digital mammography. Although it will still be a calibration-based technique, the stepwedge will no longer be required.

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