The Correlation Analysis between Breast Density and Cancer Risk Factor in Breast MRI Images

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***Abstract* – Breast cancer is one of the most common malignancy in women. Recently, the development in medical imaging technology increases the diagnosis effectiveness in predicting breast tumor in the early stage. The trend in breast cancer diagnose is to predict what kind of breast cancer could be happened instead of detecting the disease. In this paper, a breast magnetic resonance imaging is applied to compute breast density. The breast density value is used to find the correlation with the cancer risk factors such as the age, the cancer type, the tumor location, the tumor size and the cancer tumor grading. The statistics tools one-way single factor ANOVA, F-test and descriptive statistics is used to analyze the correlation. Our study found that breast density with the degree of differentiation of tumor cells in infiltrating ductal carcinoma has a significant relevance (P<0.05). Because of the result is beyond our expectation, we implied the result may be caused because of the lack of a large enough amount of testing samples. We hope that we can extend the result of this study to find out the correlation pattern to accurate assessment the risk coefficient of breast cancer by calculating breast density, and providing physicians to prognostic assessment.**

***Index Terms* – Breast Cancer, Breast MRI, Breast Density, Statistical Tools**

I. INTRODUCTION

Breast cancer is one of the most common malignancies in women. Although there is a serious threat, we can cure it effectively if it is found earlier. There are lots studies show that women will increase the risk of breast cancer about 1.8 to 6 times with higher breast density (dense breast tissue). If the physician could predict the risk of cancer cases, and assess the type of cancer, he could take preventive diagnosis and treatment that will increase the survival rate for these women. By this observation, lots of researchers addressed that breast density is an indicator to determine whether women are prone to breast cancer, or high-risk group for breast cancer.

Basically, medical imaging is the main tool for radiologists in the clinical assessment of breast density (A. Meyer-Baese, 2008). The breast medical imaging tools such as mammography, ultrasound and magnetic resonance imaging (MRI), are commonly used for physician to assess breast information. Among these image modalities, MRI can provide a strong contrast between the milk ducts, fatty tissue and other soft tissue, and can produce three-dimensional images covering the entire breast. Some literatures pointed out MRI can provide a more accurate measurement result, and is very suitable for the dense breasts measurements (Deborah J Thompson, 2009) (Julia E. E. de Oliveira, 2009).

In this paper, we handle this task with a retrospective study. We have collected the pathological data and 3D breast MRI images, and then we calculate breast density. At the same time, we also used F-test, single-factor ANOVA, and descriptive statistics to analyze the correlation between breast density and breast cancer risk factors(age), and the correlation between breast density and cancer information such as the types of cancer, tumor location, tumor size and tumor grading.

Our study found that breast density with the degree of differentiation of tumor cells in infiltrating ductal carcinoma has a significant relevance (p<0.05). Because of the result is beyond our expectation, we found that may be an error from sampling. We hope that we can extend the result of this study to find out the correlation pattern to accurate assessment the risk coefficient of breast cancer by calculating breast density, and providing physicians with prognostic assessment more accurately.

II. METHODOLOGY

A. Background

The definition of breast density is the ratio of fatty tissue to glandular (dense) tissue (Karla Kerlikowske, 2007). Some researchers addressed that breast duct is the most common site of breast cancer; it is also the indicator of estrogen increase abnormally (Klifa C, 2010). The dense breasts suffer the high-risk potential of developing breast cancer. Thus, the measurement of breast density is used to predict the probability of breast cancer (Bremnes Y, 2007).

This paper is a pilot study based on the principle of "prevention is better than cure". We compare breast density with some cancer risk factors. The breast density can predict breast cancer incidence, breast cancer in a better position to judge the information such as the type and degree of breast cancer development, and expect to be able to provide more relevant information to predict breast cancer information. With a reliable reference, the physician can conduct preventive diagnostic and treatment, and reduce the false

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positive patients with invasive biopsy in the diagnosis of breast cancer.

B. Methods

- Data source

The MRI breast images are acquired from Taipei Medical Hospital and Tungs' Taichung MetroHarbor Hospital between May 2011 and October 2011. There are totally 30 cases with image sources and pathological data. The pathological data used in this study have been granted by the Institutional Review Board (IRB). The cases are anonymized to ensure that no violation of personal privacy. Only the age of the case and pathological data, types of cancer, tumor location, tumor size and tumor grading are adopted for research. Furthermore, all pathological data in the cases are validated by professional breast specialists to ensure the accuracy of the experimental analysis.

There are 64 MRI images in each case, each image are obtained before injecting contrast medium via a 1.5T breast MRI machine using a dedicated spiral RODEO technology (Aurora System; Aurora Imaging Technology Inc., North Andover, MA, USA). The image parameters are listed as follows: Tr/Te is 28/4.8ms，rotation angle is 45 degrees, FOV is 360cm，slicing is 1.1mm，and the image size is 512 by 512.

- The breast density calculation algorithm

In this study, we developed a breast density calculation tool in MATLAB by the algorithm proposed by Chia-Hung Wei. The breast density values are then applied with the cases of pathological information for statistical comparative analysis. The flowchart of breast density computation algorithm proposed is shown as Fig. 1.

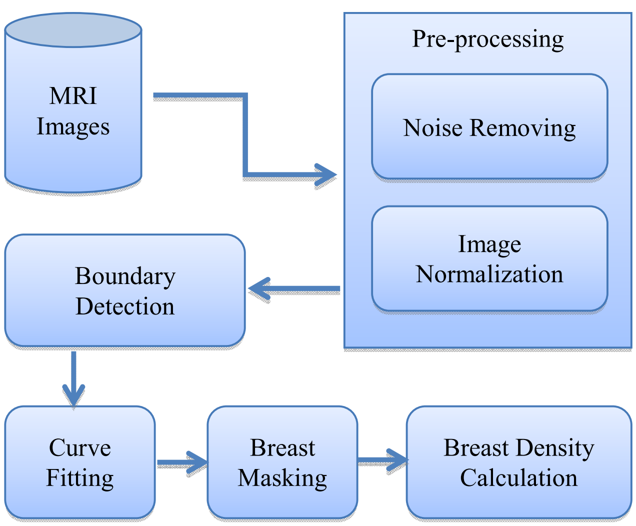


Fig. 1. The flowchart in calculating breast density

- Pre-processing

We use median filter to reduce the noise in MRI images. Then we keep the tissue area and remove the unwanted background. The morphological erosion processing is performed to remove the skin part beside breast tissue.

- Boundary detection

Given a pre-defined threshold value, the edge between breast area and the chest wall is detected. The original breast boundary is the input sample points for the further curve-fitting step to obtain a better breast boundary. The breast boundary detection result is shown in Fig. 2.

- Curve fitting

The irregular detection result in the previous step is refined by fitting the original data points to a parabolic curve as shown in Fig. 3.

- Breast masking

The breast area above the fitted curve is reserved to define the breast area of interest (AOI). Inside the breast AOI, a thresholding-based boundary detection method is used to identify breast tissue. This breast masking method keep the breast area information for further density calculation task. As shown in Fig. 4(a), the derived breast AOI is derived. The breast mask is detected from the AOI by extracting the fibroglandular tissue from breast tissue.

- Breast density calculation

In this step, an adaptive moment preserving, which improve the classic moment preserving with a thresholding adjustment method is used to determine the proper threshold. The next step is to obtain the areas of the fibroglandular tissue and the whole breast tissue. The breast density is obtained by calculated the ratio of the area of fibroglandular tissue and the whole breast area. In Fig. 4(b), we show the detection result of the fibroglandular tissue area.

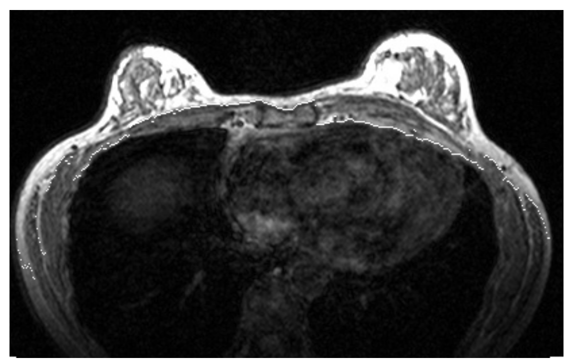


Fig. 2. The boundary detection result

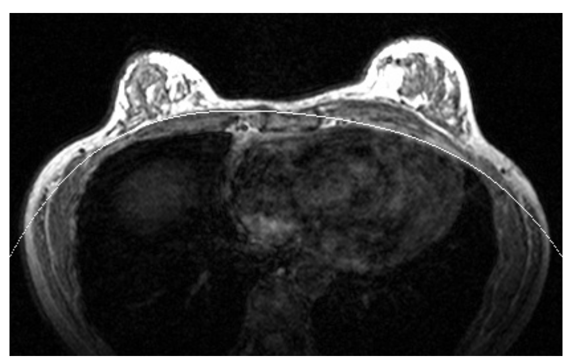
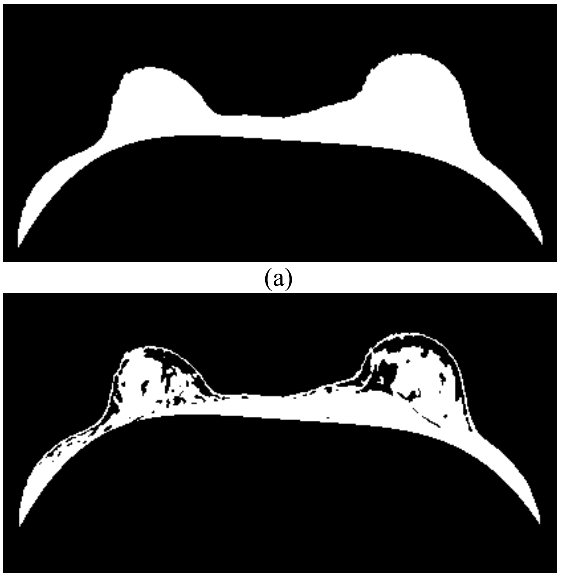


Fig. 3. The curve fitting for breast area



(a)

(b)

Fig. 4. (a) The breast mask derived from breast AOI, (b) The extracted fibroglandular tissue area by adopting an adaptive moment preserving method.

C. Statistics

In this study, the statistics analysis is carried out on SPSS 20. We analyze the correlation of breast density and cancer risk factor with one-way single factor ANOVA with confidence interval 95%. We calculate the mean and standard deviation of the variables used in this test including age, cancer type, tumor location, tumor size and tumor grading. Then the Fisher distribution test (F-test) is applied to identify the model that best fits the population from which the data were sampled. If the F ratio is greater than the critical value, it implies that the risk factor is related to breast density; otherwise the risk factor is unrelated to breast density. The definition of the cancer risk factor is defined as Table I.

TABLE I. THE DEFINITION OF THE SYMBOLS

Variables	Definitions
Age	The age while the breast cancer is confirmed
Cancer Type	The type of the breast cancer, includes: • ductal carcinoma in situ, DCIS • infiltrating ductal carcinoma • invasive lobular carcinoma
Tumor Location	The location of the tumor first occurs
Tumor Size	The actual volume of the tumor
Tumor Grading	According to the definition of Bloom-Richardson (BR) grading system, the tumors are classified with three grades, i.e. low, intermediate and high. The grade indicates how aggressive the cancer is.

To examine whether breast density is relevant to tumor size and tumor location, these two variables are also included to explore the relevance. We also choose the most frequent happened cancer types, i.e. ductal carcinoma in situ (DCIS), infiltrating ductal carcinoma and invasive lobular carcinoma as the cancer type variables, to analyze the relevance with breast density.

The scores of invasive tumors from the Bloom-Richardson grades are categorized by the standard proposed by the Collaborative Stage data collection system version (CSv2) of the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (Rubin, 2004). The higher scores indicate the higher severity of the invasive tumors. The Bloom-Richardson grading system is shown in Table II.

TABLE II. BLOOM-RICHARDSON GRADING SYSTEM

Code	Bloom-Richardson scores	Bloom-Richardson grade
1	3-5	Low
2	6,7	Intermediate
3	8,9	High

III. THE EXPERIMENTAL RESULTS

A. The Analysis of the Relevance between Breast Density and Risk Factors

In the following, we will describe the result of the variables in analyzing the correlation between breast density and cancer risk factors. The analysis result between the cancer risk factors and breast density is shown in Table III.

TABLE III. THE ANALYSIS RESULT BETWEEN CANCER RISK FACTORS AND BREAST DENSITY

Cancer Risk Factor	Critical Value	F Value	Significance Value *p*
Age	2.80	0.484	0.197
Cancer Type	3.01	0.184	0.126
Tumor Location	4.23	0.048	0.795
Tumor Size	3.39	0.278	0.193
Bloom-Richardson Scores	3.39	3.219	0.057

- Age

The F value of this variable is 0.484, is much less than the critical value 2.80 and the significance value p is 0.197 is greater than 0.05. It means that the correlation between breast density and is quite small. For the samples in this study, it means the age factor is not relevant to breast density.

- Cancer type, tumor size and tumor location

From Table III, we can find that the F values of these three variables are much less than the critical values, respectively. And the significance for each variable is also greater than 0.05. The result implies that breast density is not relevant to these three variables.

- Bloom-Richardson scores

It is worthy to note that breast density and the Bloom-Richardson scores seems reveal a relevant result. There is a little difference between the F value of the Bloom-Richardson score (3.219) and the critical value (3.39). The significance value 0.057 is also close to 0.05. For this reason, we have designed another experiment to verify the correlation between the tumor grading and breast density for further analysis and discussion.

B. The Analysis of the Relevance between Breast Density and Tumor Grading

From the previous section, we find that the tumor grading could be a relevant factor to breast density. To confirm this assumption, we use Levene's test to understand the correlation between breast density and the tumor grading. The Levene's test is an inferential statistic used to assess the equality of variances in different samples. In Table IV and Table V, we illustrate the calculated data for the Levene's Test. The distribution of Table IV is illustrated in Fig. 5.

TABLE IV. THE MEAN AND STANDARD DEVIATION FOR BLOOM - RICHARDSON GRADING CODE

Bloom-Richardson Grading Code	**Mean**	**Standard Deviation**
1	56.30	3.076
2	55.72	6.857
3	55.80	8.085

TABLE V. THE LEVENE'S TEST RESULT FOR BLOOM-RICHARDSON GRADING AND BREAST DENSITY

F Value	**Critical Value**	**Significance Value *p***
3.219	3.390	0.057

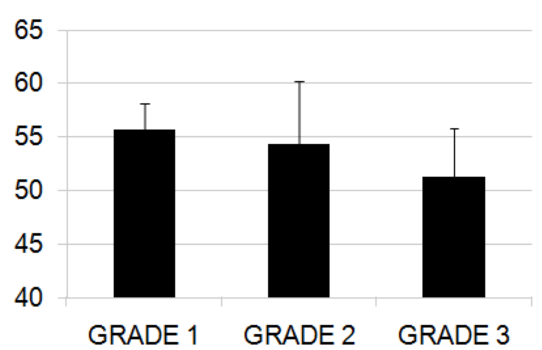


Fig. 5. The Illustration Graph for Bloom-Richardson Grading Code Distribution

As shown in Table V, the Levene's test shows that the F value 3.219 is very close to the critical value 3.390, and the significance value p is 0.057 in only slightly greater than the significance level 0.05. The result implies that the two factors, i.e. breast density and tumor grading, could have the rough correlation. However, the mean for three tumor grading (Grading Code 1, 2 and 3) is nearly equal. We conclude that there are some unknown factors affecting the sample data. To understand the possible causes to disturb the correlation between breast density and tumor grading, we add another variable, which its significance value is the secondly close to 0.05, i.e. the variable of "cancer type". We try to introduce the most popular breast cancer "infiltrating ductal carcinoma" as the subject, and analyze the data with Bloom-Richardson scores and breast density variables. The result is shown in Table VI, Table VII and Fig. 6.

TABLE VI. THE MEAN AND STANDARD DEVIATION FOR BLOOM-RICHARDSON GRADING CODE (FOR INFILTRATING DUCTAL CARCINOMA)

Bloom-Richardson Grading Code	**Mean**	**Standard Deviation**
1	55.95	3.301
2	56.13	4.408
3	55.45	8.988

TABLE VII. THE LEVENE'S TEST RESULT FOR BLOOM-RICHARDSON GRADING AND BREAST DENSITY (FOR INFILTRATING DUCTAL CARCINOMA)

F Value	**Critical Value**	**Significance Value *p***
6.893	3.52	0.006*

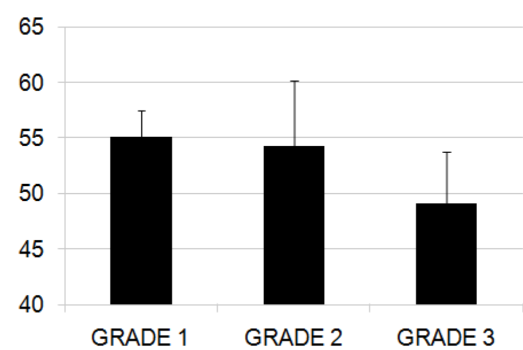


Fig. 6. The Illustration Graph for Bloom-Richardson Grading Code Distribution (for Infiltrating Ductal Carcinoma)

Table VI shows the mean and standard deviation for Bloom-Richardson grading code for infiltrating ductal carcinoma. By the result, we can find that the F value 6.893 is much greater than the critical value 3.52; it implies the null hypothesis is rejected. The significance value p is 0.006, which is much smaller than the significance level 0.05. For the infiltrating ductal carcinoma cases, Bloom-Richardson grading owns the highly relevance to breast density. However, the means for three Bloom-Richardson grades are slightly different as shown in Fig. 6. We cannot imply the conclusion that infiltrating ductal carcinoma cases have some type of correlation with Bloom-Richardson grades.

IV. Conclusion and Discussion

In this paper, we completed a pilot study for exploring the correlation between breast density and breast cancer risk factors. We adopted statistical tools such as single factor ANOVA, F-test and Levene's test to verify the relevance between these variables. The results show that although age is an important risk factor for breast cancer, this factor is not very correlated to breast density. The other variables such as cancer type, tumor location and tumor size have no strong evidence to correlate to breast density.

Our study found that breast density with the degree of differentiation of tumor cells in infiltrating ductal carcinoma has a significant relevance ($p<0.05$). Because of the result is beyond our expectation, we implied the result may be caused by the lack of a large enough amount of testing samples. If we can collect a larger number of samples with different types of breast images, which contains breast cancers and non-breast cancer tissue grading, and then conduct a comparative analysis with breast density, the conclusion about the relevance will be more clear. We hope that we can extend the result of this study to find out the correlation pattern to accurate assessment the risk coefficient of breast cancer by calculating breast density, and providing physicians to prognostic assessment.

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