

Automated Evaluation System of Japanese Mammary Gland Density Using Breast Thickness: An Initial Study

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Abstract Data in Japan shows that the risk of developing breast cancer increases after the age of 40 and peaks in the late 40s. The most common method of breast cancer screening in Japan is through mammograms, and in recent years, experts have considered combining mammograms with an ultrasound to increase the detection rate of breast cancer. Meanwhile, in the United States, physicians alert the patients of their mammary gland density after the mammogram. The physician offers the possibility of tumors being covered up by the mammary tissue, and use this data to determine the appropriate interval between check-ups. However, this advice based on mammary gland density relies on the physician's visual assessment, and reproducibility remains a challenge. Software that quantitatively evaluates mammary gland density is already commercially available, but is optimized for the Western population. This study aims for the automatic evaluation of mammary gland density of Japanese subjects. We define an evaluation index of the mammary gland amount based on the breast thickness obtained from the DICOM header, and the characteristic amount of breast tissue measured through image analysis. We verified the accuracy of the proposed indicator in its ability to correctly classify mammary gland density across 458 cases, and found it consistent with the physician's classification in 98.5% of the cases. In the future, we look to create an index to calculate average glandular dose (AGD) based on this index.

Keywords: *mammary gland density, mammary gland, breast thickness, architectural evaluation, computer-aided diagnosis*

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1. Introduction

In the ultrasound, the mammary gland is rendered white similar to a mammogram, but because breast cancer is rendered black, there is small impact on the detection of breast cancer even when the mammary gland density is high [1]. For this reason, we can expect ultrasound screenings on young patients to improve breast cancer detection rates among dense breast tissue, often missed by mammograms. [2,3] However, at present, the criteria to determine whether a subject requires an ultrasound is unclear, and it is up to the radiologist's discretion whether or not to perform the ultrasound. As a result, there is a risk of misdiagnosis, when an unnecessary test is ordered for symptoms that don't require an ultrasound, or an ultrasound is not ordered for symptoms that require an ultrasound examination. The main factors forming the basis of conducting the ultrasound are the mammary gland density as seen in the mammogram and breast thickness.

There are several systems commercially available to tackle these problems that use the mammogram to quantitatively evaluate mammary gland density. However, the evaluation is based solely on pixel values [4]. That is, since breast thickness is not considered, the system is

unable to determine whether an ultrasound is necessary. In addition, the system is optimized using the mammograms of the Western population. These points present challenges in the application to the mammograms of Japanese patients, for whom dense breast tissues are common [5]. Similarly, Asian women also have higher-density breasts [6,7]. We too have already developed a program to extract the mammary gland from a mammogram, and achieved the automatic classification of mammary gland density [8,9,10,11]. This system used analog mammograms as inputs and was capable of the automatic classification of mammary gland density, but faced challenges such as compatibility with digital mammography devices, which had quickly become widespread in recent years, and the development of a GUI for the console-based system.

Currently, the mammogram is the standard for breast cancer screening in Japan. Japan is characterized by the high rate of breast cancer among young people in comparison to Western countries [12]. Breast cancer occurs in the mammary glands, but because the mammary gland is replaced by fat with age, young patients show instead a higher mammary gland density compared to older patients, as fatty metamorphosis has not progressed in their mammary glands. Therefore, it is difficult to expect a high breast cancer detection rate like in Western

countries using only a mammogram screening. Even in the United States, currently, the physicians notify the patient of her mammary gland density following the mammogram, to present the possibility of tumors hidden in the breast tissue. Thus, the "Research on the Effectiveness of Ultrasonography in Breast Cancer Screening" was conducted in Japan, and the results were published [13]. This study conducted a comparison between a control group that used an ultrasound screening in combination with the mammogram, and a group that did not. The study elucidated the accuracy, the advantages/disadvantages, and effectiveness of the screenings in the two groups. As revealed here, ultrasonography has attracted attention as a method to complement the shortfalls of the mammogram. [14].

In this study, we will improve on our proprietary automatic classification system's evaluation method, of the mammary gland extract and mammary gland density [8,9,10,11]. These technique of the mammary gland evaluation are consists of two parts. One is the breast region detection and the others are the architectural evaluation of the mammogram. The breast region is detected by the gray value. Then, to classify the breast tissue (fat and mammary gland) by using the gray value difference in the detected breast region. Evaluation of the mammary gland will also include breast thickness as a parameter. At the same time, we will create a prototype of the mammary gland evaluation system. Through a large-scale experiment conducted through the present system, we look to evaluate the performance of the automatic mammary gland density classification system.

2. Methods

In Figure 1, we depict the flow of the automatic evaluation system for mammary gland density of Japanese patients taking into account breast thickness. In Figure 1, the segments represented by CUI1, CUI2 have been traditionally implemented in the CUI system [8,9,10,11]. Here, we conduct system integration and adaptation to digital mammograms. Then, using the breast thickness information obtained from the DICOM header, we perform an automatic evaluation of mammary gland density. The automatic evaluation of mammary gland density requires the establishment of a new formula to calculate evaluative values based on information around breast thickness in addition to the information obtained through structural evaluation (Architectural Evaluation) of the breast using a conventional method. The system indicates a mammary gland density based on this derived evaluative value.

2.1. The Implementation of the GUI Interface and System Integration

The conventional mammary gland evaluation system was a console application built in the programming language, C [8,9,10,11]. This leaves a challenge with regards to the aim of this study, an evaluation experiment by physicians. Thus, we perform the migration to a GUI application. In the present study, we realize a GUI for the system by creating a Windows Forms Application in the programming language, C#. In the development of a GUI,

we re-code the previously-developed program written in C, and add a GUI element necessary to the system. The GUI element is to include a selection button and track bar for case images to enable intuitive operation.

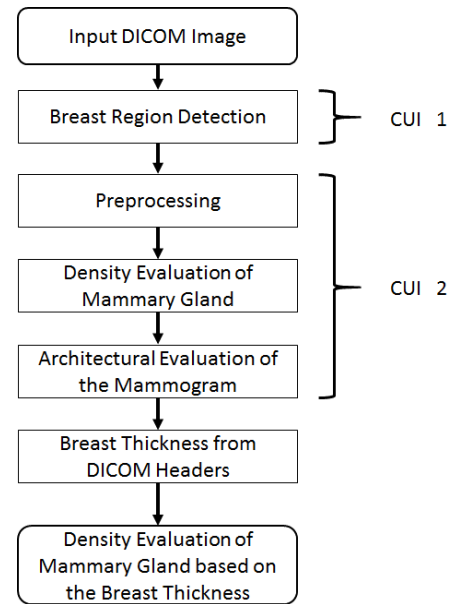


Figure 1. Flowchart of the proposed method

In addition, in the previously-developed CUI program, the program used to cut out the breast image area from the input mammogram (CUI1), and the program to evaluate the mammary gland (CUI2) were separate and independent console programs. Here, we integrated the two programs, and interfaced with one GUI application.

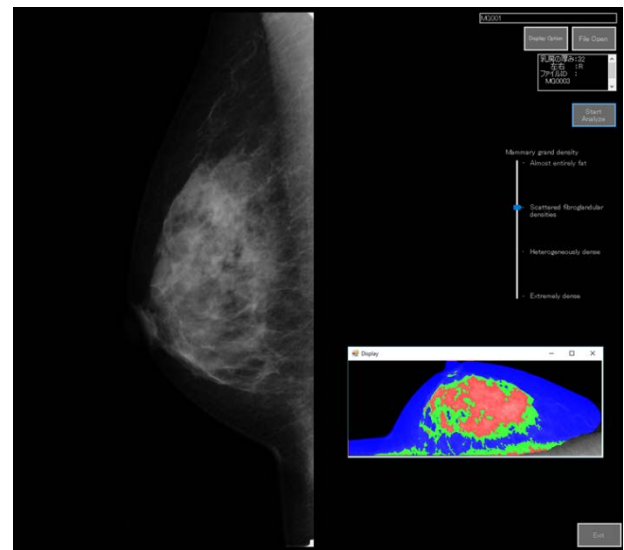


Figure 2. System interface of the proposed method

Figure 2 shows the system interface, where the input image, the digital mammogram, is open. Further, Figure 3 shows the results of the architectural evaluation of the breast obtained by system integration. In conventional systems, mammary gland evaluation had been conducted across four regions (Dmg, Dc, Db and Da) based on the proportion of each. The following shows the flow of processing. Moreover, the definition of these four regions are similar to the conventional method. Originally, the four regions had been defined as follows: the region

considered to contain the mammary gland as Dmg, the region accounting for 50% or more of the mammary glands as Dc, the region containing between 10% or more and less than 50% as Db, and the region containing a mammary gland density most closely resembling fat as Da.

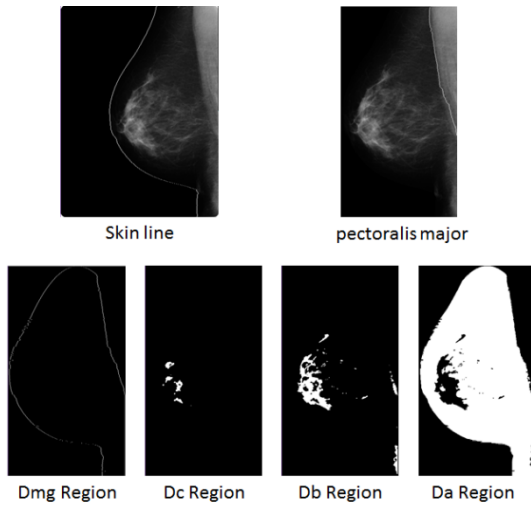


Figure 3. Architectural evaluation of the input image

The input image is the image obtained from a digital mammography device in DICOM format. First, we cut out the corresponding breast area, a procedure that pertains to CUII. We identify using the Otsu Method the breast area and background area excluding the breast. We then identify the skin line, the area of skin covering the breast (Figure 3, upper left). At the same time, within the area distinguished by the skin line (excluding the background), we use the Otsu Method to differentiate the greater pectoral muscle from everything else in the image (Figure 3, upper right). Next, we identify the Dmg area as the area described above, namely the skin line excluding the greater pectoral muscle. This assigned area becomes the region in which the mammary gland is said to exist, and becomes the standard in which to identify the regions Dc, Db, and Da. The parameters used for Dmg identification and identification methods for Dc, Db, and Da were implemented on the same basis as previous research.

Table 1. Classification table of the mammary gland density

	Dc Region	Db Region	Da Region
Almost entirely fat	0%	-	Over 90%
Scattered fibroglandular densities	0% ~25%	Over 10%	-
Heterogeneously dense	25% ~ 80%	-	-
Extremely dense	Over 80%	-	-

Next, we obtain the component ratio of the breast based on the number of pixels of each of the breast regions described above (Dc, Db, and Da regions within Dmg). Then, we conduct architectural evaluations of the breast according to the standards in Table 1. From these steps, we achieved the integration of the systems evaluating mammary gland density, something which had been implemented using CUI. In Figure 4, we show the four types of mammary glands: almost entirely fat (F), scattered fibroglandular densities (S), heterogeneously dense (HD), and extremely dense (ED), and the recognition results of the mammary gland architecture in each.

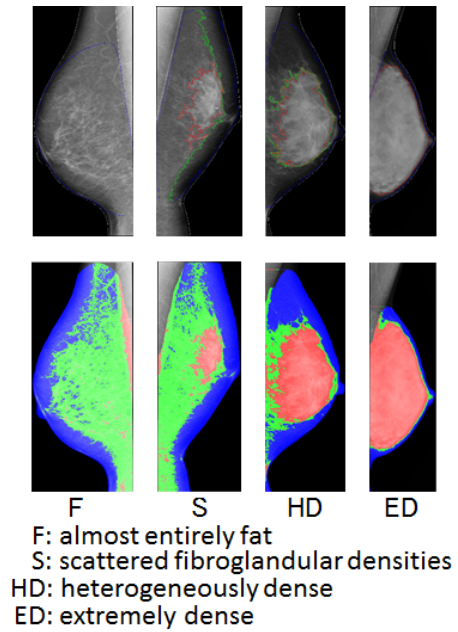


Figure 4. Evaluation results (Four types of mammary gland architecture)

2.2. Gathering Breast Thickness Information and Calculation of a Value to Evaluate Mammary Glands

The recognition results of the mammary gland architecture in the previous sections are based on conventional methods and does not consider breast thickness. Therefore, we define in this paper a new formula to calculate a value evaluating mammary glands. The formula will be based on breast thickness and the number of pixels used for automatic detection of the mammary gland architectures in the Dmg and Dc regions, as described above.

First, breast thickness information is automatically stored in the header of the image during mammography imaging. We search for "0018,11A0," the data tag containing information on breast thickness within the DICOM-format header, and extract breast thickness information contained after the tags. In Figure 5, we show the flow to obtain breast thickness data from the DICOM header.

Next, we use this breast thickness as a new parameter and add this to the classification of mammary gland architecture as obtained in the previous section. Taking into account breast thickness, we thus attempt a quantitative evaluation and classification of mammary gland density, something physicians had previously determined subjectively. In this paper, we define the evaluative value R_v , which represents the mammary gland quantity, through the following equation.

$$R_v = \frac{I(Dc)}{I(Dmg)} \times Bt \times 100 \quad (1)$$

where, function I shows the number of pixels in the region, Bt denotes breast thickness as obtained from the DICOM header. In other words, the formula takes the ratio of Dc, or the region containing 50% mammary glands, over Dmg, or the region thought to contain the mammary glands, and multiplying breast thickness to the result. As a result, the evaluative value R_v becomes a high value when the

number of pixels in the Dc region and/or breast thickness is large.

3. Experiment

In this paper, we used the FCR profectCS manufactured by Fujifilm Corp. as the mammography imaging device. We used the MLO images from 458 cases, taken between April and June 2013 by the Iwate Prefecture Preventive Medicine Association.

3.1. Calculation of Evaluative Value

We use formula (1) across the 458 cases previously mentioned to calculate the evaluative value R_v . In the West, Dance et al. have already examined breast thickness and mammary gland quantity. They have reported continuous variation in breast thickness and mammary gland quantity [15]. In the present study, we examine the evaluative value using the proposed formula (1) on the breasts of Japanese subjects.

3.2. Automatic Evaluation of Mammary Gland Density Using an Evaluative Value

On initial attempt, we classify the mammary gland quantity into three categories. Classification A includes the cases with few mammary glands, classification B includes a moderate amount of mammary glands, and classification C includes cases with many mammary glands. We attempted classification using the evaluative value R_v , derived from Formula 1. In this paper, we empirically developed the following scheme to analyze the evaluative values for classification: less than 2.0, between 2.0 or more and less than 600, and 600 or more.

4. Results and Discussions

4.1. Calculation of the Evaluative Value

Using the 458 cases, we calculated the evaluative value R_v . The results are shown in Figure 6. The horizontal axis shows the case number, and vertical axis shows the evaluative value R_v . The vertical axis is a logarithmic axis. Figure 6 shows that the evaluative value R_v , derived from mammary gland density and breast thickness, is not a continuous distribution as seen in Dance et al. Therefore, the present indicator is not a direct alternative to the AGD calculation method proposed by Dance et al.

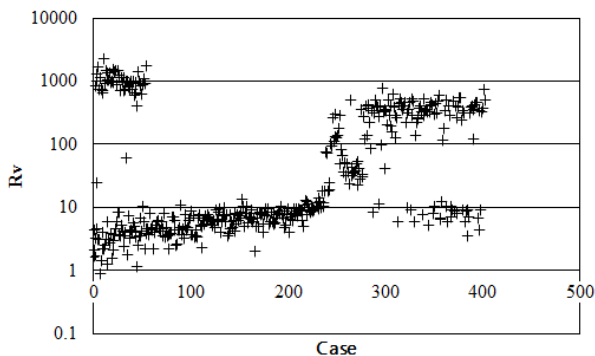


Figure 6. Calculating result of the R_v value

With regards to future challenges for the system, we look to consider a formula that can achieve more a continuous stream of evaluative values and obtain a c-factor to correct for the mammary gland content in Japanese patients.

4.2. Automatic Evaluation of Mammary Gland Density Using an Evaluative Value

In Table 2, we show the results as compared to a physician's assessment and classification of mammary gland quantity into 3 categories. Table 2 shows that the number of cases that matched between the physician and computer's classifications were as follows: 2 cases in classification A (100%), 398 cases in classification B (98.6%), and 51 cases in classification C (96.2%). As a result, the system achieved an analysis of the mammary gland with high accuracy, at a 98.5% average.

Table 2. Classification result of our proposed method using R_v value

Classification results		Proposed method		
		A	B	C
By physician	A	2	4	1
	B	0	398	1
	C	0	1	51

From this, it can be said that the system has high precision in the automatic classification of mammary gland quantity. However, the system has not yet resolved the classification of the 4 architectural types used in medicine (almost entirely fat, scattered fibroglandular densities, heterogeneously dense, extremely dense).

5. Conclusion

In this study, we targeted digital mammograms intended for ultrasound-combined screenings, and built a system to automatically evaluate mammary gland density. At the same time, we proposed a formula to output an evaluative value by which the mammary gland quantity can be classified into one of three categories. In this paper we proposed a mathematical formula dependent on breast thickness data and the gray value automatically derived from an inputted digital mammographic image. Furthermore, we compared our experiment over 458 cases with the evaluation of a physician, to show a high accuracy at a 98.5% average.

In the future, we aim to derive a formula that can calculate more continuous evaluative values of mammary gland density to make possible an index to gauge Japanese-specific mammary glandular doses.

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