Glandularity Estimation in Japanese Women by Using a Breast Model Made from Mammographic Findings of European Women

Ai KAWAGUCHI,*1, 2 Yuta MATSUNAGA,*1, 3 Yasuki ASADA,*4 Shoichi SUZUKI*4 and Koichi CHIDA*1

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This study aimed to estimate breast glandularity in Japanese women using patient exposure conditions and tissue-equivalent materials by a conventional method. Typical glandularities in Japanese women were compared with those in European women to verify the validity of the average glandular dose estimation manual based on the EUREF protocol. Glandularity was estimated from the data of 600 patients and the model breast of the tissue-equivalent materials which had various amounts of glandular contents and thicknesses. The model breasts were measured to examine the relationships between the thickness of the glandular contents and tube loading by using an automatic exposure control system. Then, equations were established to determine glandularity from patient data. The mean glandularity in the highest compressed breast thickness (CBT) group of 36–45 mm was 72%. The mean CBT of the 184 (31%) patients with glandularities exceeding 100% was 31 mm. Glandularities in patients with CBT of 30–70 mm in the present study were higher compared to those in European women by approximately 10–20%. The results suggest that the model breast of European women might not be a suitable reference standard for more than 30% of Japanese women, who have breasts with lower CBT.

KEY WORDS: mammography, breast, glandularity, average glandular dose, patient dose.

1 INTRODUCTION

In women undergoing mammography for breast cancer screening in Japan, images are acquired primarily of the craniocaudal and mediolateral oblique views of each breast. The breast comprises skin and glandular, adipose, and areolar tissues. Given that mammary glands are highly sensitive to the adverse effects of radiation, it is a prerequisite in patient dose management that the benefits of screening should considerably outweigh the risks associated with radiation.

Mammography dose is expressed as the average glandular dose (AGD), which varies according to the glandularity of breast tissue. Glandularity is defined as the percentage of glandular tissues in the breast. Standard protocols for AGD estimation include those published by the American College of Radiology (ACR) and the European Organization for Quality Assured Breast Screening and Diagnostic Services (EUREF). This model breast for European women has been used to determine the typical glandularities for AGD estimation in reference phantoms. The EUREF protocol proposes limiting values, including acceptable and achievable levels of AGD for every 10 mm of PMMA phantom thickness, ranging from 20 to 70 mm, for quality control in dosimetry; the conversion coefficients for the AGD of PMMA are based on the mean glandularities of patients between 50 and 64 years of age, as reported by DANCE et al.. In a previous study, typical
glandularities were estimated based on patient exposure conditions and tissue-equivalent materials using the model breast.5)

Average glandular dose has been used as a diagnostic reference level (DRL) 6 in mammography. The regulations define DRL as dose levels appropriate for particular reference group of patients or reference phantom. There are concerns that the AGD might vary appreciably among patients in different regions of the country.1–12) If this concern is justified, there might be regions where the benefit-to-risk ratio might be less favorable than the national average. Additionally, estimation of mean glandularity is essential for calculating the numerical value of AGD for the DRL, because a typical breast exhibits different local values of glandularity and compressed breast thickness (CBT), similar to the variations in typical height and weight among different regions and countries. Although typical glandularities estimated by the conventional method using breast models derived from the data of European women have been reported in several regions and countries,4, 5, 13–15) the typical glandularity of Japanese women has yet to be fully characterized.

This study aimed to estimate the breast glandularity of Japanese women using a previously published method 5, 13–15) based on the evaluation of patient exposure conditions and a model breast composed of tissue-equivalent materials. Breast glandularities were estimated from the digital mammographic data of 600 Japanese women examined at two different institutions. Typical glandularities in Japanese women were compared with those in European women to verify the validity of the AGD estimation manual based on the application of the EUREF protocol in a Japanese population.

II MATERIALS AND METHODS

1. Characteristics of the mammography units

Two mammography units — a computed radiography (CR) unit and a full-field digital mammography (FFDM) unit — were employed in this study to investigate the differences in distribution of glandularity due to the use of different mammography units with automatic exposure control (AEC) systems. The typical characteristics and parameters of the mammography units installed at the two institutions are shown in Table 1. The mammography units were each equipped with an AEC system and used in clinical practice.

Institution 1 used a Fuji Amulet mammography system (Fujiﬁlm, Tokyo, Japan), which is a flat-panel-based FFDM system, where one of three AEC modes—the H, L, or W-modes—can be selected. Images in lower-energy modes are acquired at higher contrast, which corresponds to higher radiation dose in mammography. The H-mode employs the least energy and highest patient dose among the three modes. The W-mode employs the highest energy and lowest patient dose. The L-mode employs a medium level of energy. Institutions can select a particular mode upon considering whether the contrast or dose should be given greater priority in order to satisfy the requirements of the doctor in charge of interpretation of mammography findings. Institution 1 employs the H-mode for imaging in clinical practice. The system acquires information related to the attenuation characteristics of the breast from the preliminary exposure (pre-exposure) data. This information is used for the determination of tube-loading value (mAs) for image acquisition, which helps determine the fixed dose value for the detector. The position of the AEC is selected automatically.

Table 1 Typical characteristics and parameters of the two mammography units.

<table>
<thead>
<tr>
<th>Institution 1</th>
<th>Institution 2</th>
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<tbody>
<tr>
<td>Fuji Amulet</td>
<td>GE Senographe DMR+</td>
</tr>
<tr>
<td>Focus–film distance (cm)</td>
<td>65</td>
</tr>
<tr>
<td>Target/Filter (Filter thickness)</td>
<td>Mo/Mo (30 µm)</td>
</tr>
<tr>
<td></td>
<td>Mo/Rh (25 µm)</td>
</tr>
<tr>
<td></td>
<td>W/Rh (50 µm)</td>
</tr>
<tr>
<td>HVL at 28 kV for Mo/Mo (mmAl)</td>
<td>0.36</td>
</tr>
<tr>
<td>AGD for 40 mm PMMA (mGy)</td>
<td>1.61</td>
</tr>
<tr>
<td>Tube voltage ranges for target/filter combinations (kV)</td>
<td>Mo/Mo 25–28</td>
</tr>
<tr>
<td></td>
<td>Mo/Rh 27–31</td>
</tr>
<tr>
<td></td>
<td>Rh/Rh 31</td>
</tr>
<tr>
<td></td>
<td>W/Rh 30–32</td>
</tr>
</tbody>
</table>

*Mo, molybdenum; Rh, rhodium; W, tungsten; HVL, half value layer; AGD, average glandular dose.

Institution 2 used a GE Senographe DMR+ system (GE Medical Systems, Milwaukee, WI, USA), which is a CR mammography system, where the operator can choose among AEC modes similar to those of the Fuji Amulet system. The Senographe system is equipped with three modes for the automated optimization of parameters (AOP), including the contrast (CNT), standard (STD), and dose (DOSE) modes. The CNT mode employs the least energy and highest patient dose among the three modes, while the DOSE mode employs the highest energy and lowest patient dose; the STD mode employs a medium level of energy. Institution 2 typically uses the STD setting. The AEC position is adjusted manually by the operator while estimating the location of high glandularity in the breast.

2. Patient data

We made application for ethical discussion to our institutional review board, and their judgement was that there is no need for their discussion since data regarding patient attributes were made anonymous in this study. Therefore, the institutional review board approval was unnecessary. For this retrospective study, we collected the data of patients evaluated between December 2011 and December 2013 at the two participating institutions. In total, 600 patients (300 women from each institution; age range, 33–81 years) who had undergone mammographic examinations were identified. The women had no previous history of breast surgery, and their compression force exceeded 100 N. For mammographic examination, images were acquired primarily of the
craniocaudal and mediolateral oblique views of each breast. In the present study, we evaluated the right craniocaudal images because the craniocaudal view corresponds to the model breast used in the Monte Carlo simulation and includes less muscle, which simplifies the process of analysis of glandularity based on exposure conditions using AEC. Data regarding patient age, CBT, tube voltage (kV), target-filter combination, and tube loading were recorded for each subject from the digital imaging and communications in medicine (DICOM) headers. As part of the quality control procedure, uncertainties in the displayed CBT were clarified by performing CBT measurement every 6 months. Uncertainties in displayed CBT for the Amulet and Senographe DMR+ systems were within errors of ±2 mm and ±3 mm, respectively.

3. Estimation of breast glandularity

Glandularity was estimated based on the patient data (CBT, target/filter and tube voltage combinations, and tube loading) as well as breast models comprised of tissue-equivalent materials (CIRS, Norfolk, VA, USA). A breast tissue-equivalent series of phantoms were manufactured to mimic both the attenuation and density of a range of glandular and adipose tissue compositions encountered in mammography. They were assembled in a variety of thicknesses (5, 10, and 20 mm) to represent compressed breast thicknesses corresponding to various glandularities in order to simulate various patient demographic characteristics. The phantoms employed in this study were prepared with five different compositions, including 100% adipose tissue, a mixture of 70% adipose tissue and 30% glandular tissue, a mixture of 50% adipose tissue and 50% glandular tissue, a mixture of 30% adipose tissue and 70% glandular tissue, and 100% glandular tissue. The tissue-equivalent materials were all rectangular in shape, measuring 10 cm × 13.5 cm in size along the axis parallel to the chest wall edge of the cassette holder. Glandularity estimation was performed using the methods employed in previous studies as references.

In clinical mammographic examination, AEC serves to maintain the signal produced for the X-ray detector. Different tissue-equivalent materials were evaluated using the two mammography units with different AECs in order to determine the relationships among thickness, beam quality (target/filter and tube voltage), tube loading, and glandularity. The position of AEC was selected automatically in the Amulet system, while that in the Senographe DMR+ system was located nearest to the chest wall. A 5-mm-thick slab of adipose-equivalent material was placed at the top and bottom of the breast phantom to represent the adipose layers described by DANCE et al. It was assumed that the adipose layers did not contribute to the overall glandularity of the phantom. Therefore, the term "glandularity" represents the percentage of glandular content in the central region of the breast phantom excluding the adipose layers. Similar to the 5-mm model, a 10-mm-thick slab of adipose-equivalent material was placed at the bottom of the breast phantom to represent the two outer adipose layers. The resultant change was confirmed to be solely in terms of position of the adipose-equivalent material, since the tube-loading values determined by the AEC systems of the two mammography units did not change. The order in which the slabs were arranged did not have a significant effect on the tube loading value.

The tube-loading values were measured under the AEC conditions of the two mammography units using tissue-equivalent materials with a range of simulated relative glandular contents (0%, 30%, 50%, 70%, and 100%) and thicknesses (20–90 mm for each 5-mm increment, including the 10-mm adipose layer), while varying the target/filter and tube voltage combinations. Variation of tube loading and thickness of the tissue-equivalent materials for each target/filter and tube voltage combination produced five forms of the following equation for glandularity values:

\[
\text{tube loading (mAs)} = \alpha \exp(bt)
\]

where \( \alpha \) and \( b \) are the least-squares fit parameters for the tube-loading values of the phantoms (each of 5-mm thickness), and \( t \) represents thickness. In addition, the equation describing the relationship between breast glandularity (g) and tube loading may have the following form for the five versions of equation (1) representing five glandularity values:

\[
g = A(t) \ln(mAs) + B(t)
\]

where \( A(t) \) and \( B(t) \) are the least-squares fit parameters for the tube-loading values of the five glandularities, after substitution of the patient’s CBT for \( t \) in the five versions of equation (1) representing the five glandularity values. Following this, the value of “g” was determined from the tube-loading values of each patient. In previous studies, equation (2) had been constructed based on the most common target/filter and tube voltage combination alone. However, in the present study, we constructed equation (2) from each target/filter and tube voltage combination under all exposure conditions. Because the equations were determined from the data of tissue-equivalent materials with thicknesses ranging from 20 mm to 90 mm, glandularity estimation could be performed in patients with CBT > 20 mm.

The average glandularities of Japanese women were compared with those of European women, reported by DANCE et al. Patients with CBT > 20 mm were divided into two groups according to age, with a cutoff of approximately 50 years. The lower age limit of 50 years approximately coincides with the menopausal age, during which significant changes in the composition of the breast are known to occur. In previous studies on glandularity and CBT, patients were divided into two groups according to the menopausal age — while one group included patients between the ages of 33 and 49 years (mean age, 43 years), the other group included those between the ages of 50 and 81 years (mean age, 60 years). In the present study, the average glandularity for each CBT was calculated and compared with the values reported by DANCE et al.
### RESULTS

**Figure 1** presents a histogram of distribution of CBT of the 600 patients. The mean CBT was 39 ± 13 mm (minimum, 7 mm; maximum, 88 mm). Glandularity could not be estimated in breasts with CBT < 20 mm \((n = 37; \text{Amulet system, 9 patients; Senographe DMR+ system, 28)}\). The mean ages of the patients with CBT ≥ 20 mm evaluated using the Amulet and Senographe DMR+ systems were 55 and 51 years, respectively.

The mean glandularity and standard deviation (SD) for each mammography unit (CBT ≥ 20 mm) are presented in **Table 2**. The SD of each mean CBT value measured using the Amulet system was lower compared to that measured using the Senographe DMR+ system. However, there was no significant difference in the distribution of glandularity of patients with CBT > 20 mm between the Amulet and Senographe DMR+ systems \((p < 0.05; \text{analysis of covariance})\).

Four patients evaluated using the Amulet system exhibited glandularities < 0%, with CBTs ranging from 53 to 88 mm. Six patients evaluated using the Senographe DMR+ system exhibited glandularities < 0%, with CBTs ranging from 35 to 64 mm. The glandularities of 80 and 104 patients evaluated using the Amulet and Senographe DMR+ systems, respectively, exceeded 100%. The mean glandularity of patients with CBTs 36–45 mm (168 patients), who formed the highest CBT group, was 72 ± 36%.

**Figure 2** presents the distribution of glandularity among the 563 patients with CBT ≥ 20 mm. The mean glandularity was 86%, and the mean CBT was 41 mm. Patients with glandularity exceeding 100% represented 33% of the 563 patients (CBT ≥ 20 mm). The 184 patients (31% of the 600 patients) with glandularity > 100% exhibited a mean CBT of 31 ± 8 mm.

**Figure 3** and **4** present the comparison of typical breast glandularities between Japanese and European women. Regression curves were applied to mean glandularities for each CBT group, excluding inaccurate mean glandularities > 100%.

**Table 2** Mean glandularity for compressed breast thickness measured using the two mammography units.

<table>
<thead>
<tr>
<th>Compressed breast thickness (mm)</th>
<th>Fuji Amulet</th>
<th>GE Senographe DMR+</th>
</tr>
</thead>
<tbody>
<tr>
<td>(20–25)</td>
<td>23</td>
<td>170</td>
</tr>
<tr>
<td>(26–35)</td>
<td>66</td>
<td>106</td>
</tr>
<tr>
<td>(36–45)</td>
<td>91</td>
<td>78</td>
</tr>
<tr>
<td>(46–55)</td>
<td>71</td>
<td>28</td>
</tr>
<tr>
<td>(56–65)</td>
<td>35</td>
<td>24</td>
</tr>
<tr>
<td>(66–75)</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>(76–85)</td>
<td>1</td>
<td>–1</td>
</tr>
<tr>
<td>(86–88)</td>
<td>1</td>
<td>–15</td>
</tr>
<tr>
<td>Total</td>
<td>291</td>
<td>272</td>
</tr>
</tbody>
</table>

\(n\), number of patients; SD, standard deviation.

The patients were divided into two groups according to age, with a cutoff of approximately 50 years. While one group (**Fig. 3** included patients between the ages of 33 and 49 years (mean age, 43 years), the other (**Fig. 4** included patients between the ages of 50 and 81 years (mean age, 60 years). The mean glandularity of patients with CBTs of 20–30 mm was > 100% in the younger age group (33–49 years of age), with the 30-mm CBT group exhibiting the highest SD of glandularity (52%). In addition, the mean glandularity of the 20-mm CBT group was > 100% in the older age group (50–81 years of age), with the 30-mm CBT group exhibiting the highest SD of glandularity (53%). In case of patients with CBTs of 30–70 mm, the glandularities observed in the present study were higher compared to those reported in European women by approximately 10–20%.

The mean glandularities for each CBT in the younger age group were higher compared to those in the older age group. The greater the CBT, the greater was the difference in glandularity observed between the age groups. In both age groups, breasts with lower CBT exhibited higher glandularities than those with greater CBT. Moreover, breasts with lower...
In each breast. This indicates that the estimated glandularity of the Senographe DMR+ system could be less accurate compared to that of the Amulet system. The inaccuracies in glandularities were reflected in the higher SD values. However, the distribution of glandularity in patients with CBT > 20 mm was not significantly different between the Amulet and Senographe DMR+ systems, which indicates that the difference in validity of mammographic measurements between the two mammography units with different AECs was negligible.

In the present study, the 10 patients’ glandularity values were below 0% for 35–88 mm CBTs. ZOETELIEF et al.\textsuperscript{14) reported that 0.7% of the 4,199 patients evaluated in their study exhibited glandularity values below zero. The authors attributed this to the low glandularity of the evaluated breasts as well as to the fact that individual adipose tissue compositions cause less attenuation than average adipose tissue compositions. The same factors resulted in 1.7% of the 600 patients in the present study exhibiting glandularity values below zero.

Of the 600 patients in the present study, 31% exhibited glandularity values > 100%. Similar values were also reported in other studies at lower CBT values.\textsuperscript{4, 14) ZOETELIEF et al.\textsuperscript{14) reported that 2.5% of 4,199 patients in the Netherlands exhibited glandularity values > 100%. The corresponding proportion observed in Japanese women in the present study is higher compared to those reported among women in other countries. DANCE et al.\textsuperscript{4) reported that, in younger women, the assumption of the presence of a 5-mm-thick adipose layer is unrealistic for very thin breasts (CBT < 25 mm), and it can lead to estimated glandularities > 100%. JANSEN et al.\textsuperscript{20) compared breast models composed of different layers, including a model with a 5-mm adipose layer, as proposed by DANCE et al.\textsuperscript{4) as well as a two-component model with 3-mm-thick adipose tissue covered by 2-mm-thick skin tissue, at different values of CBT and reported that models with greater breast thicknesses exhibited relatively less attenuation because of increased beam hardening. Additionally, Sui et al.\textsuperscript{21) reported breast skin thickness ranging from 0.87 to 2.34 mm (mean, 1.44 mm), which was lower compared to that of the breast model derived from the data of European women. In these previous studies,\textsuperscript{4, 20, 21) the mammographic measurements of small, thin breasts were more affected than those of thicker breasts by the differences between the adipose layers of real breasts and the breast model. In addition, the thickness of skin of a real breast might be lower compared to that of the breast model. In the present study, a substantial percentage of Japanese women exhibited CBT < 30 mm (25% of all patients), which was higher compared to the percentages reported among women in other countries.\textsuperscript{7, 14) Breast tissues in patients with glandularity values > 100%, which exhibited a mean CBT of 31 ± 8 mm in the present study, might not match the 5-mm-thick adipose layer breast model.

The mean glandularity of breast tissue in the Netherlands was reported to be 32%\textsuperscript{14) with a mean CBT of 58.2 mm. A study involving Malaysian women reported a mean glandularity of 48.9%\textsuperscript{13) and mean CBT of 49 mm. DONG et

**IV DISCUSSION**

This study aimed to estimate the breast glandularity of Japanese women by the conventional method. The mean glandularity of the highest CBT group (36–45 mm) was 72%. Additionally, 184 (31%) of the 600 patients included in the present study exhibited glandularity values exceeding 100%, because of which, their breast glandularity could not be estimated. The mean glandularity for each CBT in both the younger and older patient groups was higher compared to that reported in European women. The breast model derived from the data of European women was found to be unsuitable for the assessment of patients with glandularity values < 0% or > 100%.

MATSUMOTO et al.\textsuperscript{19) reported a mean CBT of 37.7 mm among Japanese women, which is consistent with the results of the present study. The low SD observed with the Amulet system for each CBT was attributable to the AEC detector of the imaging system. The Senographe DMR+ system might have been offset from the correct AEC detector position because the position of the AEC was manually selected by the operator when estimating the location of high glandularity in glandularity of the highest CBT group (36–45 mm) was 72%. Additionally, 184 (31%) of the 600 patients included in the present study. The low SD observed with the Amulet CBT were expected to exhibit higher SD in CBT.
reported that Asian women were thinner than Western women, and the mean glandularity of breast tissue among Taiwanese women was 54%, with a mean CBT of 41 mm. The mean glandularity in the present study was 86%, with a mean CBT of 41 mm. However, these values included the measurements of 184 patients with glandularities > 100%, which implies that the mean value includes inaccurate glandularity values. The mean glandularity of the highest CBT group (36–45 mm) was 72%, which could not be compared with the total mean glandularities reported in other countries. However, Japanese women evaluated in the present study, including those with thin breasts, are expected to exhibit higher glandularity and lower CBT values than women from other countries.

In the present study, patients in the younger age group exhibited higher glandularity for each CBT than those in the older group. Previous studies have also reported higher glandularity among subjects of younger ages as well as those with lower CBT. The mean glandularities of both age groups in the present study were higher in comparison with the values reported by Dance et al. The CBTs of patients with glandularity values > 100% was slightly different among the two age groups in the present study. While, patients in the younger age group (33–49 years of age) exhibited CBTs of 20–30 mm, those in the older age group (50–81 years of age) exhibited CBTs of 20 mm.

The ACR protocol recommends that the AGD of an ACR-accredited phantom should not exceed 3 mGy; however, this phantom assumes 50% glandularity. The EUREF protocol proposed limiting values, including acceptable levels and achievable levels of AGD for every 10 mm of PMMA phantom thickness, ranging from 20 to 70 mm, for quality control in dosimetry. However, the conversion coefficients for AGD of PMMA were based on mean glandularities of subjects between the ages of 50 and 64 years evaluated by Dance et al.; these values of mean glandularity were lower compared to the overall values estimated in the present study. The reference phantoms for AGD in these two major mammography protocols had lower glandularities and higher CBTs than the patients evaluated in the present study. In the Japanese manual, the procedure for determining the AGD of the 40-mm reference PMMA phantom employed a glandularity value of 50% for determining the conversion coefficient. This value is lower compared to the glandularity of the breast of a typical Japanese woman, which might result in the overestimation of the AGD by the conversion coefficient by about 10%. The DRl should be based on a suitable reference group of patients or reference phantom.

The result of the present study indicate that more than 30% of Japanese women’s breasts cannot be evaluated based on a breast model derived from the data of European women. Particularly, when the patients included in the present study were divided according to age, those with CBTs of 20–30 mm and 20 mm in the younger and older groups, respectively, exhibited glandularity values > 100%. Therefore, it is necessary to establish a new breast model with CBT < 30 mm for the estimation of glandularity and AGD. To improve the accuracy of mammographic measurements, the cutoff CBTs applied in the new breast model were determined according patient age — the cutoff value of CBT for patients below 50 years of age was < 30 mm and that for patients over 50 years of age was < 20 mm. An appropriate reference phantom should be constructed based on typical Japanese breast CBT and glandularity in order to ensure quality control. The results of the present study have demonstrated the need to establish a new breast model and typical glandularity values for reference phantoms for the evaluation of Japanese women with thin breasts in the future.

V CONCLUSIONS

The mean glandularity of the highest CBT group (36–45 mm) was 72%. The glandularities of 184 patients (31% of the 600 patients) exceeded 100%. Our findings suggest that breast models constructed based on the data of European women might not be suitable for the evaluation of mammographic parameters in more than 30% of Japanese. In addition, the estimated cutoff values of CBT of two age groups were different, with the cutoff CBT values for patients below and above 50 years of age determined to be < 30 mm and < 20 mm, respectively. The mean breast glandularities of Japanese women were higher compared to those reported for the reference phantoms for AGD in major mammography protocols.

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