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ORIGINAL ARTICLE

Can quantitative evaluation of mammographic breast density, "volumetric measurement", predict the masking risk with dense breast tissue? Investigation by comparison with subjective visual estimation by Japanese radiologists

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Abstract

Background Sensitivity to detect breast cancer (BC) is not high in a dense breast due to masking in mammography. To evaluate the breast density, a volumetric measurement system has been recently developed that measures the percent fibroglandular tissue volume (percent FGV, hereafter termed as "FG%") to the breast volume (BV). This study was designed to investigate whether evaluation using FG% can accurately predict the masking risk by comparing with the current standard method of subjective visual estimation (SVE).

Methods Using pre-biopsy mammograms of 114 cases histopathologically diagnosed with BC in our facility, SVE based on BI-RADS (5th edition) and volumetric measurements of FG% were conducted. Performance to predict the masking risk was evaluated using the area under the receiver operating characteristic curve (AUC). Relationship between these parameters and the masking risk was evaluated by the adjusted multivariate linear regression analysis.

Results The AUC of SVE values was 0.742 (95% CI 0.641–0.822), while that of FG% was as significantly low as 0.560 (95% CI 0.427–0.685) ($P = 0.0014$). The SVE values correlated with the detection of BC in mammography ($P = 0.0035$), but there was no significant relationship with FG% ($P = 0.74$). The median BV and FGV were 313 cm^3 (IQR 191–440) and 63 cm^3 (IQR 44–102), respectively. The FGV was comparable to the data for Caucasian women reported in previous studies, but the BV was one-half of the previous data.

Conclusion The current volumetric measurement system to evaluate FG% to BV was found to be insufficient in the performance to predict the masking risk in Japanese women with relatively small-sized breasts.

Keywords Breast cancer · Mammography · Masking · Volumetric measurement · Japanese

Introduction

Mammography (MG) is the only diagnostic imaging technique providing a mortality-reducing effect in breast cancer (BC) screening [1]. However, it has been demonstrated that the sensitivity of MG for the detection of BC is not high in a dense breast due to masking [Breast Imaging Reporting and Data System (BI-RADS) breast composition category 3, 58.8–77%; 4, 30.4–64%] [2–5]. Masking implies that tumors are hidden in the overlapped, dense, mammary gland tissue. It occurs due to a small difference in radiolucency between the dense mammary gland tissue and tumors and they are similarly visualized in white by MG. Since the area concealing the tumors is large, the masking risk is high in a dense

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breast. In addition, it has been shown that a dense breast increases the lifetime risk of BC itself in women [6–8]. In 70% of the US states, laws to oblige doctors to notify their patient of her dense breast have already been enacted (http://areyoudenseadvocacy.org/dense/, accessed April 7, 2018).

Various studies have also shown that Asian women develop dense breasts at a high rate [9–12]. In Japanese women, the rate of development of dense breasts (extremely dense + heterogeneously dense) is as high as 54.9–68.8%, especially in women as young as in their 40s [13]. In addition, in Japan, recommendations for the problem of "dense breast" in population-based BC screening were published in 2017 under the lead of the Japanese Association of Breast Cancer Screening [13]. These recommendations state that the precise picture of a dense breast, the effects of screening methods such as breast ultrasonography, and the approaches to accurately understand the dense breast should be investigated through the collaboration of the government and the concerned organizations.

Till date, subjective visual estimation (SVE) has been the common method for evaluating the breast density. Recently, a technique based on information obtained from digitized MG was developed to measure the fibroglandular tissue volume (FGV) and was marketed by several manufacturers. The volumetric measurement system is a highly precise method to calculate the percent FGV (FG%) to the total breast volume. It has been reported that evaluation of FG% using this method is strongly related to a risk of BC [14–17]. Meanwhile, sufficient evaluation has not been conducted on the relationship between FG% using the volumetric measurement system and the masking risk in MG to reduce the sensitivity for the detection of BC [16].

Therefore, the objectives of this study were to investigate whether the current volumetric measurement system can accurately evaluate the masking risk with dense breast tissue based on FG% and to validate the use of the "current" volumetric measurement system for evaluation of the breast density to express the degree of the masking risk, i.e., breast composition.

Materials and methods

This retrospective and observational study was approved by the Ethical Review Board at Nagoya Medical Center (Approval number, 2018-23), which waived the need for informed consent.

Case background

We selected consecutive 146 women who were histopathologically diagnosed with BC between August 2017 and February 2018 by retrospectively reviewing the histopathology records of our medical center. Of the selected women, the following were excluded from the study: 2 women who had not undergone MG, 29 women who had undergone MG using the other mammography system with which the Breast Density Measurement Software cannot be used, 1 woman who had undergone MG after biopsy, and 1 woman who had breast implant surgery. Therefore, 113 women comprising 114 cases (bilateral BCs in a woman), in whom FGV measurements were feasible based on MG taken prior to biopsy, were evaluated (Fig. 1). The evaluated women were composed of 110 Japanese, 2 Filipino, and 1 Chinese (all Asians). We obtained their clinicopathological data (age, body height, body weight, menopause status, tumor size, and histopathological diagnosis) from the electronic medical record system. In the volumetric measurement and SVE,

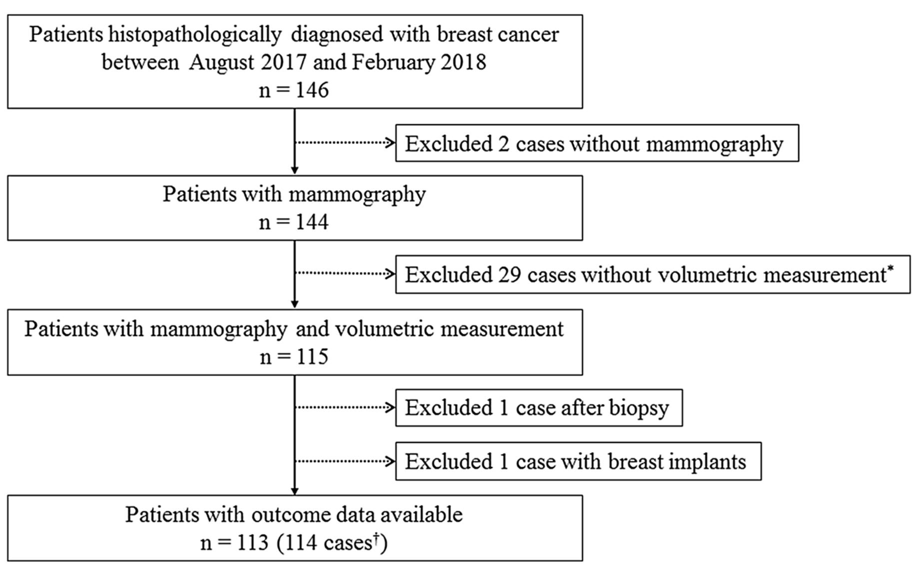

Fig. 1 Patient selection flow. Asterisk for job-related reasons in the radiology service, the women underwent MG using the other mammography system with which the Breast Density Measurement Software cannot be used. Dagger includes one bilateral breast cancer case

mediolateral oblique images on the side of the breast diagnosed with BC were used to evaluate masking.

Volumetric measurement

The mammography system used in this study was AMULET Innovality (FUJIFILM Corporation, Kanagawa, Japan). The breast density in each case was calculated as FG% by analyzing raw MG image data using the Breast Density Measurement Software in AWS v7.0 (FUJIFILM Corporation, Kanagawa, Japan). FG% was calculated as follows.

Data of the thickness of the breast at MG were obtained from the system and the FG% was estimated for each pixel based on the attenuation coefficients (mammary glands and fat) defined in advance. The volume of the mammary glands was calculated by totaling the FG% in the whole area of the breast. The volume of the whole breast, excluding the pectoralis major muscle, was also calculated to determine the ratio of the volume of the mammary glands to that of the whole breast. The ratio of the volume of the mammary glands calculated according to this algorithm was confirmed to be highly correlated with the values manually calculated from the magnetic resonance (MR) images (Pearson's correlation coefficient for FG%, 0.89, provided by FUJIFILM, unpublished data).

Subjective visual estimation

SVE was performed by four Japanese radiologists qualified with the "AS" certification from the Japan Central Organization on Quality Assurance of Breast Cancer Screening (i.e., the achieved scores required for a full-field digital mammography (FFDM) image reading instructor in Japan) and MG reading experience for at least 20 years and conducting MG soft-copy reading in the daily routine operation. SVE of the breast density in each case was performed using the following classification of the breast according to Breast Composition Categories in Breast Imaging Reporting and Data System (BI-RADS) 5th edition [18]: (a) almost entirely fatty; (b) scattered fibroglandular densities; (c) heterogeneously dense breast, which may obscure small masses; and (d) extremely dense breast, which lowers the sensitivity of MG. The breast density of each case was independently evaluated in blind by two radiologists selected for each day of the week when MG was performed according to the BI-RADS Breast Composition Categories. The four categories (a–d) were quantified with ranking 1–4, respectively, to obtain the SVE value. The categories were graded in 0.5 increments, for the median was adopted when the categories were discordant between the 1st and the 2nd reader. For example, 2.5 in the case of the 1st reader: 2 and 2nd reader: 3.

Detection of BC in MG

MG-positive cases were decided according to the review the two radiologists agreed on. The positive cases are those in whom the presence of BC was suspected on the mediolateral oblique view of MG and the area of BC on MG was consistent with the area identified on ultrasonography, magnetic resonance imaging (MRI), or histopathological findings. The MG-negative cases should not have such findings. There were no MG-negative cases with the presence of lesions in the blind area of the mediolateral oblique MG.

Imaging findings

Tumor size (major diameter, T size) was measured in MRI scans. In five cases in which MRI scans had not been taken, the T size was measured in ultrasonography scans. Among multifocal lesions, the largest lesion was measured. Features (mass or non-mass) of the lesions were assessed similarly by MRI or ultrasonography scans based on BI-RADS 5th edition.

Statistical methods

Since FG% and SVE values did not show normal distribution when assessed by the Kolmogorov–Smirnov test, nonparametric correlation coefficients (Spearman's ρ) were used for analysis.

As indices of the performance of FG% and SVE values to predict the negative detection of BC in MG, receiver operating characteristic (ROC) curves were used to calculate areas under the curves (AUCs) and 95% confidence intervals (CIs). The AUC values ranged between 0.5 and 1, and tests are judged to be sensitive when the values are closest to 1.

Multivariate linear regression analysis was performed to evaluate the relationship between FG% or SVE values and each independent factor. The detection of BC in MG (the primary focus of this study); the T size that may affect the breast density; and the age, body mass index (BMI), and compressed breast thickness, which correlated significantly with FG% and SVE values in the univariate regression analysis, were included in this analysis. The values of detection of BC in MG were 1 and -1 when the results were positive and negative, respectively, in the analysis. The menopause status was not included in this analysis since the status highly correlated with age (contribution rate in the logistic regression analysis $R^2=0.725$). The breast volume was also not included in this analysis because the volume highly correlated with the compressed breast thickness (nonparametric correlation coefficient $\rho=0.898$).

A P value < 0.05 was considered to be statistically significant.

JMP 13.2 (SAS Institute Inc., Cary, North Carolina) was used for statistical analysis.

Results

Characteristics of the BC cases

The median age of the 114 BC cases was 55.5 years. Among the cases, premenopausal women accounted for 42.1% (48 cases). The median BMI was 22.1 kg/m^2, and 25.4% (29 cases) of the women tested were overweight (BMI ≥ 25 kg/m^2). The median breast volume and FGV were 313 cm^3 [inter-quartile range (IQR), 191–440] and 63 cm^3 (IQR 44–102), respectively. The median and mean FG% were 22 (IQR 13.0–40.5) and 27.6 (SD, 18.0), respectively. The median SVE was 2.5 (IQR 2.0–3.0), and the dense breast rate was 54.4% when SVE ≥ 2.5 was considered as the dense breast. The concordance rate of BI-RADS categories observed by the readers was 65.8%. The percentage of negative detection of BC in MG was 16.7% (19 cases). The median T size in the negative detection of BC in MG was 13 mm (IQR, 8–16), and 94.7% (18 cases) were mass lesions (Table 1).

Table 1 Characteristics of the BC cases ($n = 114$)

Age[a]	55.5 [47–67]	
BMI (kg/m^2)[a]	22.1 [19.8–25.2]	
< 25	85 (74.6%)	
≥ 25	29 (25.4%)	
Menopausal status[a]		
Post-	66 (57.9%)	
Pre-	48 (42.1%)	
Compressed breast thickness (mm)	40 [26–50]	
Breast volume (cm^3)	313 [191–440]	
FGV (cm^3)	63 [44–102]	
FG%	22 [13.0–40.5]	
SVE value	2.5 [2.0–3.0]	
≥ 2.5 (as dense breast)	62 (54.4%)	
BI-RADS category	1st reader	2nd reader[b]
a	11	19
b	51	44
c	45	48
d	7	3
Detection of BC in MG		
Positive	95 (83.3%)	
Negative	19 (16.7%)	
Findings of positive detection in MG[c]		
Mass	47 (49.5%)	
Calcifications	37 (38.9%)	
Distortion	21 (22.1%)	
Asymmetry	13 (13.7%)	
Tumor size (mm)	20 [13–25]	
Positive[c]	21 [15–29]	
Negative[c]	13 [8–16]	
Findings on MRI or US		
Mass lesion	102 (89.5%)	
Non-mass lesion	12 (10.5%)	

Variable; median [inter-quartile range] or No. (%)

BC breast cancer, *FGV* fibroglandular tissue volume, *FG%* percent fibroglandular tissue volume, *SVE* subjective visual estimation, *BI-RADS* Breast Imaging Reporting and Data System, *MG* mammogram, *MRI* magnetic resonance imaging, *US* ultrasound

[a]At mammogram

[b]The readers 1st. and 2nd were not fixed readers

[C]Overlap is found

[d]Detection of BC in MG

Differences in distribution of FG% and SVE values

The histograms of the distribution of FG% and SVE values are illustrated in Fig. 2. The SVE values showed almost a bilateral symmetric distribution, whereas the FG% showed a decreasing positively skewed distribution. In the negative detection of BC in MG, the SVE values showed an increasing negatively skewed distribution, whereas the FG% showed a decreasing positively skewed distribution. The Spearman's rank correlation coefficient (ρ) was 0.589 between FG% and SVE values, indicating a moderate agreement between FG% and SVE values.

Performance to predict the negative detection of BC in MG for FG% and SVE values

The ROC curves of FG% and SVE values are plotted in Fig. 3. The AUC of SVE values was 0.742 (95% CI 0.641–0.822), whereas that of FG% was as significantly low as 0.560 (95% CI 0.427–0.685) ($P = 0.0014$) (Fig. 3).

Differences in relationship between FG% or SVE values and each independent factor

As shown by the results of the multivariate linear regression analysis, the relationship with SVE values was independently noted in terms of age ($P < 0.001$) and detection of BC in MG ($P = 0.0035$). In contrast, the relationship with FG% was noted in terms of age ($P < 0.001$), compressed breast thickness ($P < 0.001$), and T size ($P = 0.045$), but no significant relationship was noted in terms of the detection of BC in MG ($P = 0.74$) (Table 2).

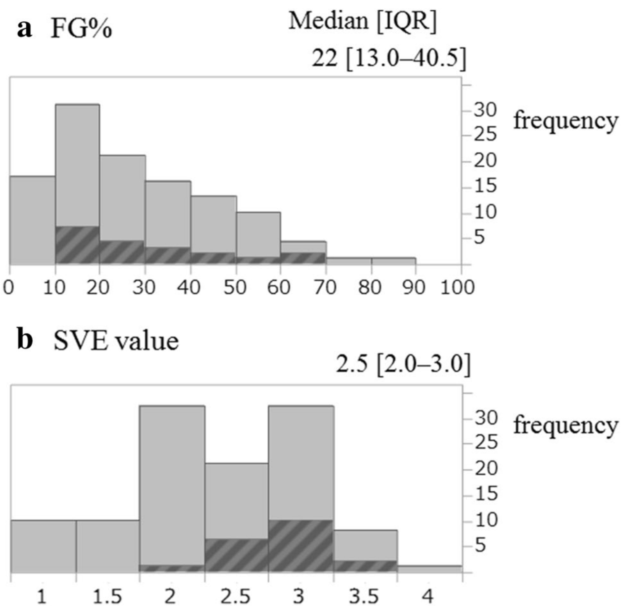

Fig. 2 Proportion of FG% and SVE value. Histograms showing the distribution of **a** percent fibroglandular tissue volume (FG%) and **b** subjective visual estimation (SVE) values ($n=114$). Coefficient of correlation between FG% and SVE, $\rho=0.589$ ($P<0.001$). Emphatic areas with slashes in the histograms correspond to the negative detection of BC in MG

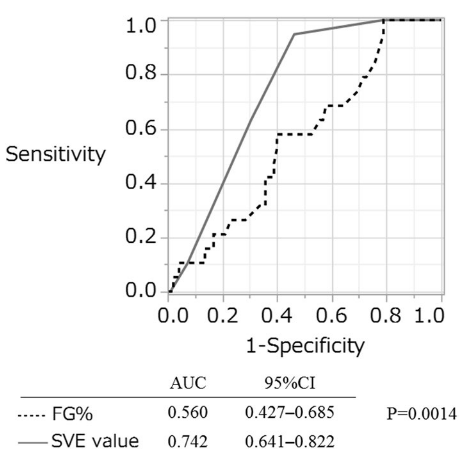

Fig. 3 Receiver operating characteristic (ROC) curves of FG% and SVE value. Negative detection of BC in MG was predicted using ROC curves (AUC) of FG% and SVE values. AUC values and 95% confidence intervals are also presented in this figure

Discussion

In this study, the FG% calculated using the volumetric measurement system showed that its performance to predict the negative detection of BC in MG was lower than the SVE values and that no significant relationship with the detection of BC in MG was observed in the adjusted multivariate analysis. In addition, the SVE values showed a symmetric distribution where the ratio of the dense breast and the non-dense breast was nearly the same, whereas the FG% showed a positively skewed distribution, indicating a significantly negative correlation with the compressed breast thickness, which was not noted in the SVE values, but noted in the FG%.

Till date, the standard method to evaluate the breast density is the classification of breast composition by SVE. However, SVE according to the gold standard of BI-RADS Breast Composition Categories has the problem of inter- and intra-observer disagreement [19–21]. The inter-observer agreement has been reported to be moderate (κ 0.43–0.54) in previous reports. It has also been reported that the intra-observer agreement was substantial (κ 0.64 and 0.71) and the variations were noted to no small extent.

Instead of using the SVE with inter- and intra-observer disagreement as mentioned above, the automated volumetric measurement system is expected to be an objective and stable evaluation method of the breast density. The volumetric measurement system is a high-precision method to calculate FG% for each pixel and FG% to the volume of the whole breast by totaling the measurement value for each pixel. This method can be incorporated into the software developed by a number of manufacturers such as Volpara (Matakina Technology, Wellington, New Zealand), Quantra (Hologic, Bedford, MA, USA), and the Breast Density Measurement Software in AWS v7.0 (FUJIFILM Corporation). The FG% calculated using the above-mentioned software showed a high correlation with values measured by MRI, which therefore confirms the precision of FG% measurement (Pearson's correlation coefficient for FG%, 0.71–0.93) [22, 23].

Several studies have reported that a dense breast increases the risk of BC in women as assessed by SVE [6–8]. Similarly, in the volumetric measurement system, it has been verified that a high FG% is a risk factor for BC. Eng et al. performed evaluation using six density assessment methods such as BI-RADS, the semi-automated Cumulus method, and the fully automated volumetric methods (Volpara, Quantra) and showed that the percent density was positively associated with BC for all methods [odds ratio (OR) for the highest vs. lowest quintile, 8.26 (95% CI 4.28–15.96), 3.94 (95% CI 2.26–6.86), and 2.96 (95% CI 0.50–17.5) for Volpara, Quantra, and BI-RADS, respectively] [14]. Brands et al. conducted a case–control study using Volpara and showed that the volumetric density was associated with the single-nucleotide polymorphism (SNP) rs 10995190 in the *ZNF365* gene, which influenced the mammographic density genetically ($P < 1.0\times10^{-6}$) and the BC risk [hormone receptor (HR) for the highest vs. lowest quartile, 2.93 (95% CI 1.73–4.96)] for the percent dense volume [15]. Park et al. conducted a study on Asian women and reported that the risk of BC increased with an increasing BI-RADS-like

Table 2 Multiple linear regression model: independent factors associated with FG% and SVE value

	FG%				SVE value			
	Estimate	Standard error	*t* value	*P* value	Estimate	Standard error	*t* value	*P* value
Age (years)[a]	− 0.397	0.095	− 4.18	< 0.001	− 0.019	0.005	− 3.95	< 0.001
BMI (kg/m^2)	− 0.599	0.387	− 1.55	0.125	− 0.031	0.020	− 1.55	0.123
Detection of BC in MG[b]	− 0.537	1.593	− 0.34	0.74	− 0.244	0.082	− 2.98	0.0035
Compressed breast thickness	− 0.726	0.119	− 6.08	< 0.001	− 0.001	0.006	− 0.24	0.81
Tumor size (mm)	0.208	0.103	2.03	0.045	0.003	0.005	0.49	0.63

FG% percent fibroglandular tissue volume, *SVE* subjective visual estimation, *BMI* body mass index, *BC* breast cancer, *MG* mammogram

[a]Age at mammogram

[b]Detection of BC in MG (1 = positive; − 1 = negative)

volumetric density grade determined using Volpara in postmenopausal Korean women [adjusted OR for volumetric density grade 4 vs. 1/2, 3.07 (95% CI 1.89–4.99)] [17]. Brandt et al. compared the classification of the breast density using Volpara and Quantra with clinical BI-RADS density classifications. They reported that the clinical and automated measures showed similar BC associations [OR for extremely dense breasts vs. scattered fibroglandular densities, 1.8 (95% CI 1.5–2.2), 1.9 (95% CI 1.5–2.5), and 2.3 (95% CI 1.9–2.8) for Volpara, Quantra, and BI-RADS classifications, respectively] and that the clinical BI-RADS assessment showed better discrimination [16]. Based on these study results, highly objective volumetric measurements are used in clinical studies as an important risk factor [Adapting Breast Cancer Screening Strategy Using Personalized Risk Estimation (ASSURE) project; EU, etc.].

On the contrary, BI-RADS 5th edition included that the Committee on BI-RADS® concludes that the association of subjectively estimated breast density with changes in the sensitivity of MG is clinically more important than the relatively smaller effect of percentage breast density as an indicator for BC risk [18]. In this study, we showed that the performance of the current volumetric measurement system, which performs risk evaluation based on FG%, was not higher than that of SVE to predict the negative detection of BC in MG, i.e., the masking risk.

A study of interval cancer using data from more than 400,000 women who participated in the Breast Cancer Screening Program has been reported by Mandelson et al. [2]. The cause of interval cancer includes technical and interpretative errors, rapid tumor growth patterns, and the extensive MG breast density. According to the results of their study, regarding the breast density visually evaluated by a radiologist using BI-RADS 3rd edition, the OR for extremely dense breasts vs. extremely fatty breasts of interval cancer ($n = 149$) adjusted for age, menopausal status, use of hormone replacement therapy, and BMI was 6.14 (95% CI 1.95–19.4). When limited to interval cancer cases confirmed by a retrospective review (excluding the cases positive on retrospective review), the OR increased to 9.47 (95% CI 2.78–32.3). These results indicate that SVE of the breast density can evaluate the masking effects well.

It has been reported that the correlation between BI-RADS-like Breast Composition Categories using the volumetric measurement system and BI-RADS Breast Composition Categories 4th edition assessed using radiologists' SVE remains at moderate agreement (κ values, 0.54–0.57 and 0.46 for Volpara and Quantra classifications, respectively) [16, 24, 25]. In studies of the volumetric breast density (same as FG%) measured by Volpara in women who received MG screening, the density was found to be 6.6–7.7% (median) in the West, whereas high values exceeding twice the Western values as 16.7% (mean) and 15.3% (median) were reported in Japan and Korea, respectively (Table 3). However, when SVE studies using BI-RADS were compared, no appreciable difference was observed in the dense breast ratio between the USA and Japan. In addition, no appreciable difference was noted in the detection sensitivity of BC in the dense breast. Therefore, the dense breast ratio between the USA and Japan extracted by SVE using BI-RADS is considered to be appropriate (Table 4). This is considered to be suggestive of a high performance of SVE using BI-RADS in the evaluation of the masking risk with dense breast tissue in Japan and is consistent with our results.

However, Destounis et al. conducted a retrospective study of screen-detected cancers ($n = 652$) and interval cancers ($n = 119$) and demonstrated that the breast density is the only independent factor related to the diagnosis of interval cancer and that the OR for extremely dense vs. fatty or scattered fibroglandular densities of all interval cancers, adjusted for age and menopausal status according to visual BI-RADS 4th edition category, was 3.60 (95% CI 1.69–7.69) and the OR for automated density grade $4 \geq 15.5\%$ vs. grade $1 + 2 < 7.5\%$ according to the automated density grade by Volpara was 3.90 (95% CI 1.99–7.64). They reported that the quantitative volumetric breast density captured the potential masking risk of breast density more accurately than visual BI-RADS [32]. In their study, the dense breast ratio of (cancer) cases

Table 3 Volumetric breast density estimates by Volpara in other studies

Study	Nation	Population	Period	No.	Age	Breast volume (cm^3)	FGV (cm^3)	Volumetric breast density (%)[a]
Brand et al. [15]	Sweden	KARMA Study Group by GE Model	2011–	19,066	54.7 (40–74)	745 [477–1090]	55 [41–75]	7.7 [5.3–11.8]
van der Waal et al. [26]	The Netherlands	Dutch breast Cancer Screening Programme	2013	992	59 [54–64]	774 [509–1119]	50 [39–70]	6.6 [4.4–10.9]
		Age group		491	(49–58)	NA	55 [42–78]	8.0 [4.9–13.2]
Brandt KR et al. [16]	USA	Medical Institution Control Subjects	2006–2012	4,170	58.0 [49.0–68.0]	NA	51.1 [37.0–71.2]	7.7 [5.0–13.2]
Moshina et al. [27]	Norway	Norwegian Breast Cancer Screening Programme	2014–2015	14,698	53.5 (50–69)	858.6 (44.0–3794.8)	52.1 (5.6–304.0)	7.4 (1.6–29.6)
Lau et al. [28][b]	Malaysia	Medical Institution Opportunistic Screening	2013–2014	915	57 [50–64]	525.4 [322.8–728.0]	43.2 [27.6–58.8]	8.9 [5.3–12.5]
Gweon et al. [24][b]	Korea	Medical Institution Opportunistic Screening	2012	778	51.7 (30–86)	380.9 (SD 204.9)	51.0 (SD 25.7)	15.4 (SD 7.8)
Youn et al. [29]	Korea	National Breast Cancer Screening Program	2013	5,697	46.2 (30–89)	344.3 [236.5–490.2]	46.9 [31.6–68.5]	15.3 [9.6–21.7]
Machida et al. [30][b]	Japan	Medical Institution Opportunistic Screening	2015	160	44.8 (22–78)	465.3 (86.1–1422.2)	68.8 (11.7–178.1)	16.7 (3.4–37.5)

Variable; median [inter-quartile range] or mean (range)

Volpara, Matakina Technologies, Wellington, New Zealand

FGV fibroglandular tissue volume, *NA* not applicable

[a]Volumetric breast density as percent fibroglandular tissue volume

[b]Opportunistic screening

(heterogeneously dense + extremely dense) according to the visual BI-RADS category was 62.9%, which was higher than the ratio of the cases in our study. However, the mean FG% was 9.5 (SD 5.5) and was much lower than our cases. The disassociation showing higher FG% values than the dense breast ratio by SVE is likely to have affected the performance to predict the masking effects.

Maskarinec et al. reported that the breast volume of Japanese women was 50% smaller than Caucasian women. Comparing the sizes of breasts among Japanese women in Japan and Japanese and Caucasian women in Hawaii, they showed that the size of the total breast differs primarily by ethnicity and the size of the dense areas differs primarily by place of residence [9]. These findings suggest that the proportion of mammary gland areas in the breast would increase in Asians whose lifestyle is westernized such as those in the present Japan and Korea. Comparing the studies of women who undertook MG screening, the FGV values were comparable between the Western countries and Japan or Korea, but the breast volume was half in Japan or Korea compared to that in the West, indicating similar results as mentioned above (Table 3). In addition, in our cases, the median breast volume and FGV were 313 cm^3 (range 191–440) and 63 cm^3 (range 44–102) cm^3, respectively, which demonstrated that the size of the mammary glands was nearly the same, but that of the breasts was one-half compared to that of Western women. Evaluation of the masking risk based on FG% is considered to be a factor for the overestimation of the risk in Japanese or Korean women with small breasts compared to that of the

Table 4 Sensitivity of screening mammography by BI-RADS breast composition categories in other studies

Study	Nation	Population	Period	No.	Age	BI-RADS edition	BI-RADS breast composition	All participants Percent (No.)	Cases of cancer Sensitivity (No.)
Kolb et al. [3]	USA	Screening	1995–2000	27,825	NA	3rd	Almost entirely fatty	51.3% (14,278)	98% (100)
							Scattered fibroglandular	48.7% (13,547)	82.9% (41)
							Heterogeneously dense		64.4% (59)
							Extremely dense		47.8% (46)
Carney et al. [4]	USA	Breast Cancer Surveillance Consortium	1996–1998	463,372	40–89	3rd	Almost entirely fatty	9.1% (42,237)	88.2% (110)
							Scattered fibroglandular	47.0% (218,129)	82.1% (975)
							Heterogeneously dense	36.0% (167,003)	68.9% (945)
							Extremely dense	7.8% (36,303)	62.2% (193)
Kerlikowske [5]	USA	US Breast Cancer Surveillance Consortium	1996–2003	1,714,351	40–69	NA	Almost entirely fatty	7.8% (133,558)	89% (256)
							Scattered fibroglandular	43.1% (773,989)	84% (2962)
							Heterogeneously dense	40.6% (696,468)	77% (3633)
							Extremely dense	8.5% (146,336)	64% (762)
Suzuki et al. [31]	Japan	Screening program in Miyagi Prefecture	1997–2002	112,071	40–69	4th	Almost entirely fatty	NA	90.7% (43)
							Scattered fibroglandular	NA	79.2% (149)
							Heterogeneously dense	NA	68.3% (104)
							Extremely dense	NA	51.1% (45)
Dense Breast Response Working Group [13]	Japan	Screening program in Fukui and Aichi Prefecture	2014	32,935	40–79	2nd[a]	Almost entirely fatty	4.7% (1,548)	NA
							Scattered fibroglandular	57.1% (18,806)	NA
							Heterogeneously dense	36.1% (11,889)	NA
							Extremely dense	2.1% (692)	NA

BI-RADS Breast imaging reporting and data system, *NA* not applicable

[a]Japanese translation of BI-RADS 2nd edition as Japanese breast composition categories by the Japan Central Organization on Quality Assurance of Breast Cancer Screening

large breast of Caucasian women because of the severe negative correlation between FG% and the compressed breast thickness and/or the breast volume as also shown in our study. If the volume of the mammary glands, which contain fat at the same proportion and therefore thought to have nearly the same masking effects, is the same, then the FG%, a percentage to the breast volume, would be double in Japanese women because their breast volume is one-half of that of Caucasian women. That is, the masking risk in Japanese women is estimated to be comparable to that in Caucasian women even if the FG% in Japanese women is twice the FG% in Caucasian women. For the purpose of evaluation of the masking risk of BC based on the mammary glands, the index values obtained by the method to determine the percentage of the mammary glands to the volume of the whole breast (FG%) may not be appropriate. Although this concern is out of the range of this study and is required to be verified in the future, the comparable dense breast ratio in Japan, obtained by SVE not affected by the breast volume, to that in the USA is supportive of this concern. Therefore, to evaluate the masking risk in women with relatively small breasts as those of Japanese women, the proportion of fibroglandular and adipose tissues in the mammary glands is important and it would be necessary to analyze whether the density of fibroglandular tissue is sufficient to hide masses as well as the masking effects.

Recently, it was shown that the evaluation of masking effects increased due to the use of the percent area where the dense tissue thickness exceeded 1 cm (PDA) [33]. The index values, such as the dense breast ratio, in the localized areas are useful to evaluate the risk that BC is masked by the localized mammary glands, and such index values may provide a prospective technique to solve problems common to the volumetric measurement system.

Limitation

There are some limitations in this study. The first is that no information was available about reproduction and the use of hormone replacement therapy, which are believed to have an impact on breast density. That is why these factors were not included in the multivariate analysis. However, we believe that this does not affect the results of the study because these factors do not appear to differently affect the two assessment methods. The second limitation is that this is a retrospective single-center study, making it impossible to completely eliminate unintended selection bias. In addition, all mammograms were taken by a single machine in this study. Therefore, our findings need to be verified by a multicenter study, in which we hope to make a comparison with the results obtained using similar volumetric measurement methods, Volpara and Quantra.

Conclusions

In this study population, the classification of breast composition by SVE was superior in performance to evaluate the masking risk, but there were disagreements between the readers. The current volumetric measurement system for evaluating the percentage of fibroglandular tissue to the whole breast was insufficient in the performance to evaluate the masking risk for the relatively small-sized breasts of Japanese women.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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