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Reproducibility of automated volumetric breast density assessment in short-term digital mammography reimaging

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Two automated volumetric breast density analyses of 44 patients who underwent image-guided needle localization in one breast were compared to calculate the agreement of assessment parameters in short-term digital mammography reimaging. The outputs of the automated volumetric breast density method included four parameters [fibroglandular tissue volume (Vfg), total breast volume (Vb), volumetric breast density (Vbd), and area breast density (Abd)]. The variability and agreement of each parameter were calculated in serial mammograms. There was no significant difference in mean Vfg, Vb, Vbd, or Abd between two mammograms ($P =$ .249, .053, .727, and .603, respectively).

1. Introduction

Mammographic breast density is defined as the relative proportion of radiopaque areas (fibroglandular tissue) within the entire breast. Many studies reported that a higher mammographic density increases the risk of breast cancer in both Western and Asian women [1–5]. Therefore, mammographic density has been proposed as a variable for individual risk assessment [6].

Several studies have shown evidence that therapies influencing hormone levels such as tamoxifen can change both mammographic density and the risk of breast cancer [7–9]; furthermore, changes in breast density on mammography have been increasingly used to monitor the effects of treatment [7–10]. However, to promote the widespread use of mammographic density change as a surrogate biomarker of treatment effect, it is essential to establish the validity of the density assessment. Traditionally, the Breast Imaging Reporting and Data System (BI-RADS) density categories or visual and computer-aided estimations of percentage density are commonly used to assess mammographic density [11–14]. However, the assessment of breast density by humans is limited by low-to-intermediate reproducibility [15–17]. The reproducibility of breast density estimates could be improved by using automated or semiautomated techniques. Recently, several methods for fully automated volumetric estimations of breast density have been used [18–21]. These models showed variable results in predicting the risk of breast cancer compared to area-based measurements of breast density [19,20]. Although only limited studies have focused on the reproducibility of this technique, those studies were performed with a relatively longer time interval or various combinations of machines which limited value of their results [22,23].

Therefore, the aim of this study was to compare the reproducibility of volumetric breast density assessment parameters in short-term reimaging performed on the same digital mammography equipment.

2. Materials and methods

2.1. Subjects and mammograms

This retrospective study was approved by the Institutional Review Board of our institution, and the requirement for informed consent was waived. We searched our records from January 2014 to February 2014 for patients who underwent mammography- or sonography-guided needle localization in one breast. To be included in this study, patients had to have undergone image-guided needle localization after routine mammography that was performed on the same mammography unit no more than 2 months apart with availability of two sets of automated volumetric density analyses of the affected breast. Between the two mammography examinations, patients were not treated with any systemic therapy or breast surgery. We excluded patients who had a history of previous surgery on the eligible breast or the use of hormone replacement therapy. We also excluded patients who underwent image-guided needle localization of more than two sites to avoid the effects of hemorrhage on quantitative density measurements and effects related to technical deficits of the mammogram, such as inadequate positioning. Finally, a total of 44 breasts in 44 patients (mean age, 50.0

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years; range, 31–79 years) were identified. Only one breast per patient was chosen for analysis.

All mammograms in this study were performed using the same full-field digital mammography system (Selenia Dimensions, Hologic Inc., Bedford, MA, USA). All mammograms were acquired in standard craniocaudal (CC) and mediolateral oblique (MLO) projections using automatic optimization of acquisition parameters.

Three (6.8%) of 44 image-guided needle localizations were performed under mammographic guidance, while the others were performed under sonographic guidance. All patients underwent image-guided needle localization for nonpalpable breast lesions, and 9 (20.5%) of 44 lesions proved to be benign. The mean interval between the first and second mammograms was 13.2 days (range, 3–56 days).

Since positioning differences could be a major factor affecting discrepant results in density assessments on serial mammograms [24], three technicians performed each mammogram included in this study while referencing previous mammograms to avoid dissimilar positioning.

2.2. Automated volumetric breast density assessments

For volumetric breast density analyses, raw image data were sent to a dedicated server running volumetric breast density analysis software (Quantra Version 2.0; Hologic Inc., Bedford, MA, USA). Briefly, this software provides fibroglandular tissue volume and total breast volume from a two-view mammogram and calculates volumetric breast density as the ratio of these parameters. The algorithm uses acquisition parameters such as tube voltage, tube current, compression thickness, and attenuation coefficients of different breast tissues to estimate the thickness of parenchymal and/or adipose tissue that the X-ray beam penetrated to deposit a given amount of energy on the detector. The Quantra software output includes fibroglandular tissue volume (Vfg), total breast volume (Vb), volumetric breast density (Vbd), and area breast density (Abd) (Fig. 1). Using volumetric measurements, Quantra also provides BI-RADS-like scores, referred to as quantized density (Q_abd) (Fig. 1). A dedicated breast radiologist with 9 years of experience (K.E.S) reviewed and recorded those quantitative data displayed on picture archiving and communication system.

2.3. Statistical analysis

We calculated the absolute and relative differences for each of four volumetric breast density parameters (Vfg, Vb, Vbd, and Abd) between two consecutive examinations. The absolute difference was the absolute value of the relative difference between serial mammograms. The relative difference was defined as the difference in percent density obtained by subtracting the percent density assessed at the second mammogram from the percent density at the first mammogram. For example, if the percent densities assessed at the first mammogram and second mammogram were 10% and 20%, the relative difference would be −10%, and the absolute difference would be 10%. A Wilcoxon signed rank test was used to evaluate significant differences between the mean volumetric breast density parameters from the first and second examinations. Kappa statistics were used to test for agreement between the first and second Q_abd. The intraclass correlation coefficient (ICC) was measured to test the agreement between the four volumetric breast density parameters on the two serial mammograms. Spearman's correlation coefficients were determined for the consecutive measurements. Differences in the Spearman's correlation coefficients of Vbd and Abd were tested for statistical significance using Fisher's z transformation.

SPSS version 19 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. $P < .05$ was considered statistically significant.

	1/29/2014						
	Total	R	L	RCC	RMLO	LCC	LMLO
Quantra	V2.0						
Vfg (cm3)	245	133	112	133	115	112	67
Vb (cm3)	1098	546	552	544	546	552	460
Vbd (%)	22	24	20	24	21	20	15
Abd (%)	35	39	30	41	38	36	24
Vbd-score	1.26	1.26	0.79	1.38	1.14	1.07	0.51
Vfg-score	0.58	0.58	0.18	0.66	0.5	0.47	-0.11
Q_abd	3	3	3	3	3	3	3
q_abd	3.34	3.34	2.97	3.43	3.25	3.2	2.73

Fig. 1. The output of automated volumetric breast density assessment program.

3. Results

Volumetric breast density parameters calculated from the first and second mammograms are shown in Table 1. There was no significant difference in mean Vfg, Vb, Vbd, or Abd between the first and second mammograms ($P = .249$, .053, .727, and .603, respectively). The mean absolute differences of serial Abd values were higher than those of Vbd values (3.43 vs. 1.91). The median absolute differences of serial Abd values were also higher than those of Vbd values (3.00 vs. 1.00). The mean absolute differences of serial Vfg and Vb values were 14.91 and 47.00, respectively. The kappa value for the two BI-RADS-like scores (Q_abd) was 0.744, showing substantial agreement (Table 2).

The mean ICC value was 0.974 for Vfg [95% confidence interval (CI), 0.953–0.986; $P < .001$], 0.990 for Vb (95% CI, 0.981–0.994; $P < .001$), 0.982 for Vbd (95% CI, 0.967–0.990; $P < .001$), and 0.985 for Abd (95% CI, 0.972–0.992; $P < .001$). All parameters showed excellent agreement and were statistically significant (Fig. 2).

Spearman's correlations between the two examinations for each parameter are shown in Fig. 3. All parameters demonstrated high Spearman's correlation coefficients greater than 0.9, which were statistically significant and showed strong correlations. However, the difference in Spearman's correlation coefficients between Vbd and Abd was not statistically significant ($P = .507$).

4. Discussion

Mammographic density is well known as a general marker of breast cancer risk [3,24]. Cuzick et al. showed in their nested case–control study that a change in mammographic density over 12–18 months is an excellent predictor of response to tamoxifen in a preventive setting [7]. Furthermore, a recent retrospective study using quantitative imaging analysis software to assess mammographic density showed that

Table 1
Variability of automated volumetric breast density assessment parameters from serial mammograms

	Mean	S.D.	Median	Min	Max	*P* value
Vfg (cm^3)						
1st examination	102.25	69.90	79.00	11.00	318.00	.249
2nd examination	99.89	73.40	76.50	18.00	377.00	
Relative difference	2.36	22.66	2.50	−88.00	58.00	
Absolute difference	14.91	17.08	8.00	0.00	88.00	
Vb (cm^3)						
1st examination	576.02	314.50	558.50	106.00	1837.00	.053
2nd examination	561.55	299.97	518.50	138.00	1741.00	
Relative difference	13.73	61.18	12.50	−185.00	125.00	
Absolute difference	47.00	40.93	39.50	1.00	185.00	
Vbd (%)						
1st examination	18.84	10.39	17.50	5.00	42.00	.727
2nd examination	18.89	10.29	16.00	4.00	41.00	
Relative difference	−0.05	2.74	0.00	−6.00	8.00	
Absolute difference	1.91	1.94	1.00	0.00	8.00	
Abd (%)						
1st examination	28.45	16.94	24.00	1.00	59.00	.603
2nd examination	28.20	17.20	25.00	1.00	62.00	
Relative difference	0.11	4.19	0.00	−9.00	9.00	
Absolute difference	3.43	2.36	3.00	0.00	9.00	