Breast compression parameters and mammographic density in the Norwegian Breast Cancer Screening Program

Authors: Nataliia Moshina ¹ Marta Roman ¹ Gunvor G. Waade ² Sofie Sebuødegård ¹
Giske Ursin ^{1,3,4} Solveig Hofvind ^{1,2}

Affiliations:

1 Cancer Registry of Norway, Oslo, Norway

2 Oslo and Akershus University College of Applied Sciences, Faculty of Health Science, Oslo, Norway

3 Institute of Basic Medical Sciences, Medical Faculty, University of Oslo, Oslo, Norway

4 Department of Preventive Medicine, University of Southern California, California, USA

Nataliia Moshina, MD, MSc

Cancer Registry of Norway, Oslo, Norway

Address: P.O. 5313 Majorstuen, 0304, Oslo (Norway)

Phone: +47 23 33 39 89

Email: Nataliia.Moshina@kreftregisteret.no

Marta Roman, PhD

Cancer Registry of Norway, Oslo, Norway; Norwegian Resource Centre for Women's Health, Oslo University Hospital, Oslo, Norway

Address: P.O. 5313 Majorstuen, 0304, Oslo (Norway)

Phone: +47 23 33 39 84

E-mail: mroman@parcdesalutmar.cat

Gunvor G. Waade, MSc

Oslo and Akershus University College of Applied Sciences, Oslo, Norway

Address: P.O. 4, St. Olavs plass

0130 Oslo (Norway)

Phone: +47 67 23 66 71

Email: gunvor.waade@kreftregisteret.no

Sofie Sebuødegård, MSc

Cancer Registry of Norway, Oslo, Norway

Address: P.O. 5313 Majorstuen, 0304, Oslo (Norway)

Phone: +47 23 33 39 83

Email: Sofie.Sebuodegard@kreftregisteret.no

Giske Ursin, MD, PhD

Cancer Registry of Norway, Oslo, Norway; Institute of Basic Medical Sciences, Medical Faculty, University of Oslo, Oslo, Norway; Department of Preventive Medicine, University of Southern California, California, USA

Address: P.O. 5313 Majorstuen, 0304, Oslo (Norway)

Phone: +47 22 45 13 27

Email: Giske.Ursin@kreftregisteret.no

Solveig Hofvind, PhD

Cancer Registry of Norway, Oslo, Norway; Oslo and Akershus University College of Applied Sciences, Faculty of Health Science, Oslo, Norway

Address: P.O. 5313 Majorstuen, 0304, Oslo (Norway)

Phone: +47 23 33 39 87

E-mail: Solveig.Hofvind@kreftregisteret.no

Abstract

Objectives: To investigate possible associations between breast compression parameters, including compression force and pressure, compressed breast thickness and breast volume, and mammographic density assessed by an automated software.

Methods: We obtained data on breast compression parameters, absolute and percent dense volume and body mass index (BMI) for 12,898 women screened with two-view (craniocaudal, CC, and mediolateral oblique, MLO) digital mammography in the Norwegian Breast Cancer Screening Program, 2014-2015. Spearman correlation coefficient and linear regression were used to study the associations between breast compression parameters, and absolute and percent dense volume, adjusting for age and BMI.

Results: Compression force, compressed breast thickness and breast volume were positively correlated with absolute dense volume ($\rho = 0.20, 0.27$ and 0.53 for left CC and $\rho = 0.14, 0.33$ and 0.45 for left MLO, respectively). Compression pressure was inversely correlated with absolute dense volume ($\rho = -0.48$ for left CC and $\rho = -0.28$ for left MLO). In the adjusted analyses, the strongest associations were observed between compression pressure and absolute dense volume, breast volume and absolute dense volume, and between compressed breast thickness and percent dense volume.

Conclusions: Breast compression parameters might affect automated mammographic density estimates.

Key words: breast; mammography; screening; breast compression; mammographic density

Key points:

- 1) Compression pressure was inversely correlated with absolute dense volume
- 2) Breast volume was positively correlated with absolute dense volume

- 3) Compressed breast thickness was inversely correlated with percent dense volume
- 4) Breast compression parameters influence automated density estimates

Abbreviations

CC – craniocaudal

MLO – mediolateral oblique

BMI – body mass index

VDG – Volpara Density Grade

BI-RADS – Breast Imaging-Reporting and Data System

SD – standard deviation

Introduction

Fibroglandular tissue appears radiographically bright on the mammogram, while fatty tissue is dark. Mammographic density reflects the amount of fibroglandular tissue in the breast and can be presented as percent or absolute density [1]. Percent density is the proportion of the fibroglandular tissue estimated in the area or volume of the whole breast, while absolute density is the actual area or volume of fibroglandular tissue. High mammographic density is a risk factor for breast cancer [2], and tumours are less visible in dense compared to fatty breasts due to masking [3].

Breast compression at mammography may influence mammographic density estimates as compression pulls the liquid out of the breast, changing mammographic appearance [4]. Compression force (newton, N) is applied when the breast is placed between the bucky and a paddle of the x-ray machine during the imaging procedure [5; 6]. Application of compression force immobilizes the breast and reduces breast thickness, which limits scatter effects, thus improving image quality, and decreases the amount of radiation absorbed in glandular tissue [5]. Compression pressure (kilopascal, kPa), defined as compression force divided by the breast area in contact with the paddle, reflects the applied compression force distribution over the breast [7; 8], while compressed breast thickness (millimetre, mm) implies the thickness of the compressed breast as measured at exposure. Breast volume (cm^3) is a volumetric estimation of the size of the breast subjected to compression based on data obtained from an automated software [9].

Measures of compression pressure and compressed breast thickness depend on compression force and a woman's pain threshold and breast characteristics, including total volume of the breast and volume of dense and fatty tissue [10]. Compression force is set by the radiographers and the magnitude of the force is associated with the radiographer's preferences

[11; 12]. Therefore, the values of breast compression parameters may differ not only between women, but also within one screening examination of four images [7; 13]. As far as we are aware, there is no evidence of the optimal values of breast compression parameters whether to achieve the best image quality or to provide the gentlest examinations with no or minimum pain. To obtain such evidence, possible associations between breast compression parameters need to be examined.

Previous studies have shown compression force and compressed breast thickness to be correlated with mammographic density [14-16]. However, further studies including a larger number of examinations are needed in order to verify the results. As a part of the amendment of the Norwegian Breast Cancer Screening Program, VolparaTM [17], an automated method for estimating absolute and percent dense volume, was installed at three of the 30 screening units. We took advantage of the collected data on breast compression parameters and mammographic density and investigated the associations. The parameters of breast compression include compression force, compression pressure, compressed breast thickness and breast volume.

Materials and methods

This descriptive study on breast compression and density parameters was performed on data from women screened in the Norwegian Breast Cancer Screening Program between 2014 and 2015. The study was approved by the Regional committee for health research ethics (2016/938).

The Norwegian Breast Cancer Screening Program

The organized screening program for breast cancer in Norway is administered by the Cancer Registry of Norway and run according to European guidelines [5]. As of 2016, about 600,000

women aged 50-69 years are invited biennially to two-view, craniocaudal (CC) and mediolateral oblique (MLO), mammography. The average participation rate is 75% for each invitation [18]. The program performs independent double reading with consensus. Between 2006 and 2015, the women received a questionnaire on selected breast cancer risk factors, including weight and height, along with the invitations. Information collected as a part of the invitation and screening examinations, including data from the questionnaire, is registered and stored at the Cancer Registry of Norway.

Study Population

We received a file with de-identified data extracted from the Cancer Registry database. Information was available for 17,867 women screened with full field digital mammography in Rogaland, Hordaland and Akershus counties, as a part of the screening program, June 2014 – May 2015. To simplify analyses, we restricted the study to women with four images at one screening examination ($n = 16,382$). We excluded information from women who did not report weight and/or height in the questionnaires ($n = 3,484$). This left information from 12,898 women available for analyses.

Measurement of study parameters

During the study period, GE Senographe Essential was used in Rogaland and Hordaland, while Philips MicroDose SI was used in Akershus. The values of compression force and compressed breast thickness were obtained from the Digital Imaging and Communications in Medicine (DICOM) header. VolparaTM (version 1.5.0) was used to estimate compression pressure, absolute dense volume (cm^3), total volume of the breast (cm^3) and percent dense volume (%) for each image taken [19]. The software provided a score of Volpara Density Grade (VDG) based on percent dense volume, which imitated the BI-RADS (Breast Imaging-Reporting and Data System) classification of mammographic density. The categories of VDG

corresponded to the following ranges of percent dense volume: VDG-1: <4.5%; VDG-2: 4.5-7.49%; VDG-3: 7.5-15.49%; and VDG-4: $\geq 15.5\%$ (26). Body mass index (BMI) was calculated as kg/m^2 based on the data on weight and height of the women obtained from the questionnaire. BMI was assigned to each of the four images of the corresponding woman.

Statistical analysis

The mean, standard deviation (SD), median and ranges of compression force, compression pressure, compressed breast thickness, BMI, breast volume, and absolute and percent dense volume were estimated for CC and MLO. Further, to identify possible differences in breast compression parameters by percent dense volume, we stratified mean and median values of breast compression parameters by VDG. The correlations between compression force, compression pressure, compressed breast thickness, BMI, breast volume, and absolute and percent dense volume were measured using Spearman correlation coefficient (ρ). Scatterplots with locally weighted smoothing were used to graphically display the relationships between the studied parameters. Absolute and percent dense volumes were lognormally distributed. We performed linear regression analyses to study the association of compression force, pressure and compressed breast thickness with natural log transformed absolute and percent dense volume, adjusting for breast volume, age (continuous) and BMI (continuous). Because of concern that the associations could be modified by BMI we performed linear regression analyses stratified by four BMI groups (< 20; 20-24.9; 25-29.9; and $\geq 30 \text{ kg/m}^2$). All variables included in regression analyses were standardized. The estimated regression coefficient of standardized variables represented the change in the number of SDs of the outcome variable (absolute and percent dense volume) on the transformed scale associated with one SD change in breast compression parameters. All analyses were conducted using STATA[®] 14.0 (StataCorp, Texas, USA).

Results

Mean compression force was 123.5 N for left versus 123.0 N for right CC mammograms, and 135.8 N for left versus 136.2 N for right MLO mammograms. Only results from the left breast are shown in the further to avoid duplex numbers. Results for both breasts are displayed in Appendix I.

Among the 12,898 women, mean age was 60.2 (SD: 5.5) years and mean BMI was 25.5 (SD: 4.1) kg/m² (Table 1). The means of breast compression parameters and absolute dense volume differed statistically significantly for left CC and MLO. The mean and median percent dense volume were similar for CC and MLO (6.5% and 5.3%, respectively).

Table 1.

Study parameters for left craniocaudal (CC) and mediolateral oblique (MLO) mammograms among 12,898 women screened in the Norwegian Breast Cancer Screening Program, 2014-2015

	CC		
	Mean (SD)	Median	Range
Compression force (N)	123.5 (25.1)	120.0	29-206
Compression pressure (kPa)	15.8 (6.4)	14.6	3.4-61.9
Compressed breast thickness (mm)	57.4 (11.8)	58.0	12-99
Breast volume (cm ³)	855.5 (412.9)	795.0	50.7-2787.5
Absolute dense volume (cm ³)	48.4 (24.9)	42.9	6.1-272.0
Percent dense volume (%)	6.5 (3.8)	5.3	1.5-35.1
	MLO		
	Mean (SD)	Median	Range
Compression force (N)	135.8 ^a (30.0)	130.0	38-206
Compression pressure (kPa)	10.7 ^a (3.3)	10.3	2.9-37.6
Compressed breast thickness (mm)	59.6 ^a (13.3)	60.0	13-100
Breast volume (cm ³)	998.8 ^a (482.1)	928.2	39.0-3524.8
Absolute dense volume (cm ³)	55.6 ^a (27.4)	49.4	3.9-341.1
Percent dense volume (%)	6.5 (3.8)	5.3	1.3-45.3

^a P<0.001 for a t-test comparison for means between CC and MLO

Stratified analyses of breast compression parameters by VDG, showed a decrease in compression force and an increase in compression pressure by increasing density (p for trend <0.001 for both) (Table 2). Compressed breast thickness and breast volume decreased by increasing VDG (p for trend <0.001 for both).

Table 2.

Breast compression parameters for left craniocaudal (CC) and mediolateral oblique (MLO) mammograms by Volpara Density Grade (VDG) among 12,898 women screened in the Norwegian Breast Cancer Screening Program, 2014-2015

	VDG-1 (n=4,293)		VDG-2 (n=5,107)		VDG-3 (n=3,002)		VDG-4 (n=496)	
	CC							
	mean (SD)	median	mean (SD)	median	mean (SD)	median	mean (SD)	median
Compression force (N)	127.2 (24.8)	120.0	124.1 (25.3)	119.0	118.6 (24.5)	116.0	115.0 (21.4) ^a	114.0
Compression pressure (kPa)	13.0 (4.8)	12.2	15.9 (6.0)	14.9	18.7 (7.3)	17.5	20.3 (7.5) ^a	18.7
Compressed breast thickness (mm)	64.3 (8.7)	64.0	57.6 (10.1)	58.0	49.8 (11.4)	50.0	42.2 (11.2) ^a	41.5
Breast volume (cm ³)	1132.7 (393.6)	1075	825.8 (347.1)	770.3	581.1 (282.8)	531.8	422.2 (223.2) ^a	370.4
	MLO							
	mean (SD)	median	mean (SD)	median	mean (SD)	median	mean (SD)	median
Compression force (N)	140.4 (29.5)	130.0	136.8 (29.9)	132.0	129.2 (29.0)	125.0	124.8 (28.6) ^a	120.0
Compression pressure (kPa)	9.5 (2.6)	9.2	10.8 (3.1)	10.5	11.9 (3.5)	11.4	12.9 (4.2) ^a	11.9
Compressed breast thickness (mm)	68.5 (9.4)	68.0	59.4 (10.9)	59.0	50.1 (12.2)	50.0	41.5 (11.1) ^a	41.0
Breast volume (cm ³)	1337.1 (456.3)	1280.6	957.8 (393.3)	895.9	670.3 (329.8)	612.6	480.2 (249.7) ^a	435.0

^aP for trend <0.001

Compression force was positively correlated with compression pressure, compressed breast thickness, breast volume and BMI ($p < 0.001$ for all) (Figure 1). Contrary, compression pressure was negatively correlated with compressed breast thickness, breast volume and BMI ($p < 0.001$ for all). Compressed breast thickness was positively correlated with breast volume and BMI ($p < 0.001$ for all). Breast volume was positively correlated with BMI ($p < 0.001$). Among the breast compression parameters, the correlations were rather weak ($\rho < 0.50$), except for those between compression pressure and breast volume, compressed breast thickness and breast volume, and breast volume and BMI ($p < 0.001$ for all).

Craniocaudal

Mediolateral oblique

Fig. 1. The relationship between breast compression parameters (compression force, compression pressure, compressed breast thickness and breast volume) and body mass index (BMI) for left craniocaudal (CC, upper panels) and mediolateral oblique (MLO) mammograms (lower panels). Each point corresponds to one compression (n=12,898 for CC and n=12,898 for MLO). The line corresponds to the locally weighted scatterplot smoothing. Spearman correlation coefficient (ρ) is shown for each relationship ($p<0.001$ for all).

The correlation between compression force, compressed breast thickness, breast volume and absolute dense volume was positive, while the correlation between compression pressure and absolute dense volume was inverse ($p<0.001$ for all) (Figure 2). The correlation between compression force, compressed breast thickness, breast volume and percent dense volume was inverse, and the correlation between compression pressure and percent dense volume was positive ($p<0.001$ for all).

Fig. 2.

The relationship between breast compression parameters (compression force, compression pressure, compressed breast thickness and breast volume) and percent and absolute dense volume for left craniocaudal (CC, upper panels) and left mediolateral oblique (MLO) mammograms (lower panels). Each point corresponds to one compression ($n=12,898$ for CC and $n=12,898$ for MLO). The line corresponds to the locally weighted scatterplot smoothing. Spearman correlation coefficient (ρ) is shown for each relationship ($p < 0.001$ for all).

The values of R-squared indicated that compression force and pressure explained very low proportions of variances of absolute and percent dense volume (Table 3). After mutual adjustment, including age and BMI, the strongest associations were observed for compression pressure and absolute dense volume, breast volume and absolute dense volume, and

compressed breast thickness and percent dense volume. No association was observed between compressed breast thickness and absolute dense volume, and between breast volume and percent dense volume in the adjusted analyses.

Table 3.

Association between breast compression parameters (compression force, compression pressure, compressed breast thickness and breast volume) and absolute and percent dense volume among 12,898 left craniocaudal (CC) and left mediolateral oblique (MLO) mammograms

	CC					
	Crude			Adjusted ^a		
	Beta ^b (95% CI)	P	R ²	Beta ^b (95% CI)	P	R ²
Absolute dense volume						
Compression force (N)	0.24 (0.22; 0.25)	<0.001	0.04	0.21 (0.19; 0.23)	<0.001	0.37 ^c
Compression pressure (kPa)	-0.43 (-0.44;-0.42)	<0.001	0.23	-0.33 (-0.35;-0.31)	<0.001	
Compressed breast thickness (mm)	0.31 (0.30; 0.33)	<0.001	0.09	-0.01 (-0.02; 0.04)	0.43	
Breast volume (cm ³)	0.58 (0.56; 0.60)	<0.001	0.28	0.35 (0.31; 0.39)	<0.001	
Percent dense volume						
Compression force (N)	-0.13 (-0.15;-0.11)	<0.001	0.01	-0.06 (-0.08;-0.04)	<0.001	0.40 ^c
Compression pressure (kPa)	0.26 (0.25; 0.28)	<0.001	0.09	0.09 (0.07; 0.11)	<0.001	
Compressed breast thickness (mm)	-0.57 (-0.59;-0.56)	<0.001	0.31	-0.50 (-0.52;-0.48)	<0.001	
Breast volume (cm ³)	-0.55 (-0.56;-0.53)	<0.001	0.27	0.03 (-0.01; 0.06)	0.14	
	MLO					
	Crude			Adjusted ^a		
	Beta ^b (95% CI)	P	R ²	Beta ^b (95% CI)	P	R ²
Absolute dense volume						
Compression force (N)	0.13 (0.11; 0.15)	<0.001	0.02	0.13 (0.11; 0.15)	<0.001	0.25 ^c
Compression pressure (kPa)	-0.51 (-0.53;-0.48)	<0.001	0.09	-0.35 (-0.39;-0.30)	<0.001	
Compressed breast thickness (mm)	0.33 (0.31; 0.34)	<0.001	0.13	0.03 (0.01; 0.06)	0.02	
Breast volume (cm ³)	0.42 (0.39; 0.42)	<0.001	0.21	0.31 (0.28; 0.35)	<0.001	
Percent dense volume						
Compression force (N)	-0.17 (-0.19;-0.16)	<0.001	0.03	-0.11 (-0.13;-0.09)	<0.001	0.44 ^c
Compression pressure (kPa)	0.60 (0.57; 0.63)	<0.001	0.11	0.30 (0.26; 0.34)	<0.001	
Compressed breast thickness (mm)	-0.57 (-0.59;-0.56)	<0.001	0.36	-0.43 (-0.46;-0.41)	<0.001	
Breast volume (cm ³)	-0.57 (-0.58;-0.55)	<0.001	0.36	-0.02 (-0.05; 0.01)	0.22	

^a Including compression force, compression pressure, compressed breast thickness, breast volume, body mass index (BMI) and age; adjusted covariates are not shown for BMI and age

^b Beta coefficients represent the difference in each measure of percent or absolute dense volume in the number of standard deviations (SDs) on the natural log transformed scale associated with one SD change in the explanatory variable

^c R-squared for the model

The results did not differ across BMI groups. Tests of heterogeneity for whether the associations between breast compression parameters and absolute and percent dense volume differed between BMI groups did not differ statistically significantly (results not shown).

Discussion

We identified associations between breast compression parameters and absolute and percent dense volume among 12,898 women aged 50-69 years, who were screened in the Norwegian Breast Cancer Screening Program between 2014 and 2015. Moderate correlations were observed between compression pressure and absolute dense volume, and between breast volume and absolute dense volume. Absolute dense volume decreased when compression pressure increased and increased when breast volume increased. A strong correlation was found between compressed breast thickness and percent dense volume. Percent dense volume decreased when compressed breast thickness increased.

Mean values of breast compression parameters for CC and MLO differed statistically significantly (Table 1 and Table A1). The difference might be related to the variation in the volume of the breast subjected to compression. MLO includes a substantially larger part of the pectoral muscle compared with CC. The pectoral muscle is not used in the estimation of either absolute or percent dense volume despite it affects breast compression, by increasing breast thickness and thus resulting in higher compression force [20; 21].

The associations between breast compression parameters, and absolute and percent dense volume may be explained by the impact of total breast volume. Breast volume was positively correlated with absolute dense volume and inversely correlated with percent dense volume. Radiographers apply higher force to large breasts [11; 22]. Compared to women with small breasts, women with large breasts tend to have higher dense and considerably higher fatty area and therefore lower percent density [23]. In volumetric terms, this indicates that women with large breasts have higher absolute dense volume, considerably higher volume of fatty tissue and thus lower percent dense volume compared to women with small breasts. Given that women with large breasts tend to receive higher compression force compared to women

with small breasts, higher compression force is related to higher absolute and lower percent dense volume. Use of site specific compression force might have influenced the strength of the correlation between compression force and breast volume as a wide compression force variation between the Norwegian breast centres has been shown in a recent study [24].

Compression pressure was inversely correlated with absolute dense volume and positively correlated with percent dense volume. Women with large breasts have lower pressure compared with women with small breasts. The lower pressure was thus related to high absolute dense volumes. Contrary, percent dense volume was lower in large versus small breasts, which might indicate a connection between low pressure and low percent dense volume. These findings were corroborated by the variation of compression pressure by categories of VDG, where we observed an increase in mean and median values of compression pressure with increasing density category. In a study investigating the association between breast stiffness, computed as a ratio of compression force and deformation of the breast due to compression, and the risk of breast cancer, it has been shown that dense volume, percent dense volume and breast tissue stiffness were positively associated with the risk of breast cancer [25]. This might indicate that low compressibility of the breast tissue, corresponding to a high level of compression pressure, is associated with high percent dense volume.

The correlation between compressed breast thickness and absolute and percent dense volume might also be linked to breast volume. Volpara estimated breast volume based on the values of compressed breast thickness and breast area contacting the compression paddle. Given the same breast area, high compressed breast thickness implies larger breast volume compared to low compressed breast thickness. Larger breast volume is related to higher absolute dense volume, which indicates that higher compressed breast thickness is associated with higher

absolute dense volume. However, large breast volume also implies high volume of fatty tissue. Therefore, percent dense volume, estimated as a ratio between absolute dense volume and breast volume, is lower for breasts with larger volume and also for high compressed breast thickness.

Our findings are in line with results from previous studies [14-16]. As such, compression force and compressed breast thickness have been shown to be positively correlated with absolute dense volume [16]. Further, inverse correlations between compression force and percent mammographic density and between compressed breast thickness and density, reported using semi- and fully automated methods of density assessment, support our findings [15; 16].

As far as we are aware, changes in absolute or percent dense volume observed within one woman, one breast or one mammographic projection due to the application of different compression forces have not previously been reported. The influence of change in compressed breast thickness on the estimates of percent dense volume has been reported in one phantom study and in one study investigating simulated errors in compressed breast thickness [26; 27]. Both studies used the same automated software as used in our study. In the study describing the development of a phantom to test an automated software for density assessment, it was assumed that application of compression force and reducing the phantom thickness caused both reduction and increase in phantom's percent dense volume [27]. These findings might indicate that the radiographers, who set values of compression force, could influence the estimates of percent dense volume by applying less or more compression force. Further, the study investigating differences in percent dense volume due to simulated errors found that both categorical density values (VDG) and percent dense volume could become different for the same woman with 15% error in compressed breast thickness [26]. These findings

correspond well to our results regarding the strong association between compressed breast thickness and percent dense volume.

Volumetric methods of mammographic density estimation are considered more accurate with respect to determining breast density and associated with it breast cancer risk compared with visual methods of mammographic density assessment [28-30]. However, our findings suggest that the studied breast compression parameters may influence volumetric density measurements and might therefore affect the accuracy of the density estimates and possibly confound the association between mammographic density and breast cancer risk. In future studies, we will include information about breast cancer to get further knowledge about this issue.

One of the strengths of our study is a large sample of mammograms from a population-based breast cancer screening program. Further, as far as we know, this is the first study that examines the relationship between compression pressure and absolute and percent dense volume. Furthermore, the study included mammograms performed by different pairs of radiographers ($n = 424$), which makes the results generalizable. One of the limitations of our study is lack of information indicating the individual radiographers and their experience in mammography, which is shown to be of influence for the compression force used in mammography screening [11; 12]. We assumed the estimates produced by the automated density measurement software to be the reference standard in our study. However, to calculate absolute dense volume, breast volume and percent dense volume, the software uses values of compressed breast thickness [19; 26]. The associations between compressed breast thickness and absolute and percent dense volume created by the software manufacturer could have affected the results of the adjusted analyses. As such, the associations between compressed

breast thickness and absolute dense volume, and between breast volume and percent dense volume have disappeared in the adjusted analyses.

In conclusion, our study identified moderate correlations between compression pressure and absolute dense volume, and between breast volume and absolute dense volume, as well as a strong correlation between compressed breast thickness and percent dense volume. Breast compression parameters, including compression pressure, compressed breast thickness and breast volume, might have an impact on mammographic density estimates obtained from the automated software.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We would like to thank Hilde Trå Hervig and Gry Rosseid, radiographers at the breast diagnostic centre of Stavanger University Hospital, Berit Hanestad, radiographer at the breast diagnostic centre of Haukeland University Hospital, and Evy Gran, head of the department of breast cancer diagnostics at Akershus University Hospital, for help and support in collecting and processing the density data used in this study. The study was supported by a grant from the Norwegian Breast Cancer Society, funded by Extrastiftelsen (2013-2-0280).

References

- 1 Kopans DB (2006) Mammography and the Normal Breast. *Breast imaging*. Lippincott Williams & Wilkins, pp 357-363
- 2 McCormack VA, dos Santos Silva I (2006) Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. *Cancer Epidemiol Biomarkers Prev* 15:1159-1169
- 3 Mandelson MT, Oestreicher N, Porter PL et al (2000) Breast density as a predictor of mammographic detection: comparison of interval- and screen-detected cancers. *J Natl Cancer Inst* 92:1081-1087

- 4 Carp SA, Selb J, Fang Q et al (2008) Dynamic functional and mechanical response of breast tissue to compression. *Opt Express* 16:16064-16078
- 5 Perry N BM, de Wolf C, Tornberg S, Holland R, von Karsa L. (2006) European guidelines for quality assurance in breast cancer screening and diagnosis, 4 edn. European Communities, Luxemburg
- 6 Williamson A, Hoggart B (2005) Pain: a review of three commonly used pain rating scales. *J Clin Nurs* 14:798-804
- 7 Branderhorst W, de Groot JE, Highnam R et al (2015) Mammographic compression--a need for mechanical standardization. *Eur J Radiol* 84:596-602
- 8 de Groot JE, Branderhorst W, Grimbergen CA, den Heeten GJ, Broeders MJ (2015) Towards personalized compression in mammography: a comparison study between pressure- and force-standardization. *Eur J Radiol* 84:384-391
- 9 Hartman K, Highnam R, Warren R, Jackson V (2008) Volumetric Assessment of Breast Tissue Composition from FFDM Images. In: Krupinski EA, (ed) *Digital Mammography: 9th International Workshop, IWDM 2008 Tucson, AZ, USA, July 20-23, 2008 Proceedings*. Springer Berlin Heidelberg, Berlin, Heidelberg, pp 33-39
- 10 Poulos A, Rickard M (1997) Compression in mammography and the perception of discomfort. *Australas Radiol* 41:247-252
- 11 Mercer CE, Hogg P, Szczepura K, Denton ERE (2013) Practitioner compression force variation in mammography: A 6-year study. *Radiography* 19:200-206
- 12 Wilkinson J. SM, Sønnesyn M. V., Gullien R., Sagstad S., Hofvind S. (2014) Kompresjonskraft i mammografiscreeningen i Oslo [Compression force in mammography screening in Oslo]. *Hold Pusten*:11-15
- 13 Kopans DB (2008) Basic physics and doubts about relationship between mammographically determined tissue density and breast cancer risk. *Radiology* 246:348-353
- 14 Khan-Perez J, Mercer C, Bydder M et al (2013) PB.10: Breast compression, compressed breast thickness and volumetric breast density. *Breast Cancer Research* 15:P10
- 15 Olson JE, Sellers TA, Scott CG et al (2012) The influence of mammogram acquisition on the mammographic density and breast cancer association in the Mayo Mammography Health Study cohort. *Breast Cancer Res* 14:R147
- 16 Khan-Perez J, Harkness E, Mercer C et al (2014) Volumetric Breast Density and Radiographic Parameters. In: Fujita H, Hara T, Muramatsu C, (eds) *Breast Imaging: 12th International Workshop, IWDM 2014, Gifu City, Japan, June 29 – July 2, 2014 Proceedings*. Springer International Publishing, Cham, pp 265-272
- 17 Matakina Technology Limited. VolparaSolutions – Volpara Density. Available via <http://volparasolutions.com/solutions/volparadensity/>. Accessed October 1 2015
- 18 Hofvind S, Geller B, Vacek PM, Thoresen S, Skaane P (2007) Using the European guidelines to evaluate the Norwegian Breast Cancer Screening Program. *Eur J Epidemiol* 22:447-455
- 19 Highnam R BM, Yaffe MJ, Karssemeijer N, Harvey J (2010) Robust Breast Composition Measurement - Volpara™ In: Martí J OA, Freixenet J, Martí R., (ed) *Lecture Notes in Computer Science: 10th International Workshop on Digital Mammography*. Springer-Verlag Berlin Heidelberg, pp 342–349
- 20 Dustler M, Andersson I, Brorson H et al (2012) Breast compression in mammography: pressure distribution patterns. *Acta Radiol* 53:973-980
- 21 Dustler M (2016) Pressure distribution in mammography. *Mechanical imaging and implications for breast compression* Medical Radiation Physics, Malmö. Lund University, Faculty of Medicine, Lund University, pp 84

- 22 Mercer CE, Hogg P, Lawson R, Diffey J, Denton ER (2013) Practitioner compression force variability in mammography: a preliminary study. *Br J Radiol* 86:20110596
- 23 Stuedal A, Ma H, Bernstein L, Pike MC, Ursin G (2008) Does breast size modify the association between mammographic density and breast cancer risk? *Cancer Epidemiol Biomarkers Prev* 17:621-627
- 24 Waade GG SA, Hofvind S (2016) Compression force and radiation dose in the Norwegian Breast Cancer Screening Program. *Eur J Radiol.*
<http://dx.doi.org/doi:10.1016/j.ejrad.2016.12.025>
- 25 Boyd NF, Li Q, Melnichouk O et al (2014) Evidence that breast tissue stiffness is associated with risk of breast cancer. *PLoS One* 9:e100937
- 26 Waade GG, Highnam R, Hauge IHR et al (2016) Impact of errors in recorded compressed breast thickness measurements on volumetric density classification using volpara v1.5.0 software. *Med Phys* 43:2870-2876
- 27 Waade GG, Hofvind S, Thompson JD, Highnam R, Hogg P Development of a phantom to test fully automated breast density software – A work in progress. *Radiography.* 10.1016/j.radi.2016.09.003
- 28 Shepherd JA, Kerlikowske K, Ma L et al (2011) Volume of mammographic density and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 20:1473-1482
- 29 Gubern-Merida A, Kallenberg M, Platel B, Mann RM, Marti R, Karssemeijer N (2014) Volumetric breast density estimation from full-field digital mammograms: a validation study. *PLoS One* 9:e85952
- 30 Wang J, Azziz A, Fan B et al (2013) Agreement of Mammographic Measures of Volumetric Breast Density to MRI. *PLoS One* 8