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Towards personalized compression in mammography: A comparison study between pressure- and force-standardization

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ABSTRACT

Objective: To compare a conventional 14 decanewton (daN) force-standardized compression protocol with a personalized 10 kilopascal (kPa) pressure-standardized protocol.
Methods: A new add-on contact area detector, which enables pressure-standardized compression, is validated in a double-blinded intra-individual comparison study. Breast screening participants (433) received one craniocaudal (CC) and one mediolateral oblique (MLO) compression for both breasts. Three of these compressions were force-standardized, and one, blinded and randomly assigned, was pressure-standardized. Participants scored their pain experience on an 11-point numerical rating scale (NRS). Three experienced breast-screening radiologists, blinded for compression protocol, indicated which images required retakes.
Results: An unanticipated under-compression issue that occurred at forces below 5 daN was effectively solved with minimal extra radiographer training during the study. For pressure-standardized compressions obtained at 5 daN or more, the compressed breasts thickness increased on average 4.2% (MLO)—6.3% (CC), average pain scores were reduced by 10% (MLO)—17% (CC) and the proportion of women experiencing severe pain (NRS $\geq$ 7) was reduced by 27% (MLO)—32% (CC), compared with force-standardized compressions (all p-values <0.05). Average glandular dose (AGD) and proportions of retakes were similar for both protocols.
Conclusion: Pressure-standardized compressions resulted in AGD values and a retake proportion similar to force-standardized compressions, while pain was significantly reduced.

1. Introduction

In mammography, flattening of the breast reduces dose [1,2] and improves image quality [3–6]. However, these so called "breast compressions" are also associated with discomfort and pain [7,8]. The 2008 Cochrane systematic review found adverse effects [9–12] for several pain reducing strategies [11–14] and concluded that further research is called for [9]. There are also large variations in compression forces used between countries [15] ["this issue"] and between radiographers [16] (also called mammography technologists or breast imagers). One reason for these variations may be that mammography quality assurance guidelines worldwide [6,17] only mention subjective compression criteria such as "until the skin is taut at the sides" [18].

A recent observational study in a Dutch hospital [19] showed that women with small breasts significantly more often experienced severe pain than women with large breasts. We found that this is because the compression protocol of this hospital stated that the same target force should be applied to each breast, regardless the size of the breast. In this "force-standardized" approach, smaller

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breasts get much higher *pressures* (force per unit of contact area) than larger breasts. For that purpose, we developed a personalized compression protocol in which the same pressure is applied to each breast. This corresponds to applying forces that are proportional to the individual breast contact areas. Since women with smallest breasts experience most pain, it makes sense that less force is used for them, as is done in many countries and screening programs where there is no obligation to aim for a specified target force. What is new in our "pressure-standardized compression" approach is that we propose to *standardize* breast compression based on pressure, which at the same time may achieve pain reduction [19,20].

Pressure is expressed in the SI unit kilopascal ($1\,kPa = 1\,daN/1\,dm^2 \approx 7.5\,mmHg$). Since pressure is defined as "total force divided by contact area", it can be considered a breast "personalized" version of force. Pressure has the same physical dimension as tissue elasticity (Young's modulus) and blood pressure, whereas force itself is unrelated to any physiological parameter. Therefore, pressure may be more closely related to physiology than force. Since current mammography devices cannot measure the applied pressure in real time, we developed an add-on radiolucent contact area detector that enables compression to any desired target pressure.

The aim of this paper is to validate the use of a pressure-standardized compression protocol with a 10 kPa (75 mmHg) target pressure. This is done by comparing the compressed breast thickness, average glandular dose (AGD), pain experience, and the proportion of required retakes with respect to a strict implementation of the 14 daN target force compression protocol used in Dutch screening.

2. Materials and methods

2.1. Subjects and study design

This double-blinded intra-individual comparison study was performed in a breast cancer screening unit in Apeldoorn, the Netherlands. Approval was obtained from the Committee for Population Screening of the Health Council of the Netherlands [21]. We invited all women scheduled for a screening mammogram on 28 study days. Those who had previous breast treatment and those who did not understand the study information due to language or intellectual disability were excluded and received a regular mammogram. Participants ($n = 433$) aged 49–75 years (mean 60.2 ± 7.8 standard deviation), provided written informed consent. Each participant received a standard mammographic examination consisting of one craniocaudal (CC) and one mediolateral oblique (MLO) compression for both breasts. Of these four compressions, three were performed with the 14 daN force-standardized protocol, and one, blinded and randomly assigned, with the personalized 10 kPa (75 mmHg) pressure-standardized protocol. With the intention to maximize reproducibility (standardization), the radiographers aim to reach the target compression level as precisely and accurately as possible. However, less compression is used if the woman indicates that she considers the procedure too painful.

To prevent order-effect bias, a custom computer program provided a randomized order of compressions based on a predefined list; starting with the left breast as often as the right, starting with the two CC-compressions as often as with the two MLO-compressions and having the pressure-standardized compression equally often first, second, third and last. Since image quality and AGD of pressure-standardized mammography has not been validated before, the study was performed in two phases with a halfway evaluation of the available data. In the evaluation of phase 1, we identified an unanticipated technical issue leading to under-compression at low forces (explained in results). The cases with low forces will therefore be analyzed separately and presented alongside the complementary cases. To prevent this issue in phase 2, we implemented two measures: (i) a minimum force of 6 daN, and (ii) extra training for the radiographers. In the first phase ($n = 214$), the pressure-standardized protocol was always applied to one of the CC-compressions, and in the second phase ($n = 219$) always to one of the MLO-compressions. With this study design, each pressure-standardized compression has one force-standardized compression on the contralateral breast in the same view (CC/MLO), as well as two force-standardized control compressions in the other view (MLO compressions in phase 1 and CC compressions in phase 2).

2.2. Data acquisition

All compressions were performed on the same calibrated mammography device (Selenia S, Hologic Inc., Bedford, MA, USA). For performing the force-standardized compressions, we recorded breast thickness and applied force from the mammography device throughout each breast compression, as described in [19]. To enable pressure-standardized compressions, we also recorded the contact area by equipping both the small (18×24 cm) and large (24×30 cm) paddles with radiolucent and calibrated detector sheets (described in Appendix A). The ratio of applied force and contact area was continuously calculated to estimate the contact pressure at each moment of the compression. A custom display (see Fig. 1a) showed the compression level as percentage of the blinded target value, but not the actual values themselves. A team of five mammography screening radiographers, each with at least 2.5 years of experience, was instructed to compress the breast until the compression level was 100%. In this way, both the radiographers and the women were blinded for which protocol was used. All participants were instructed to hold their breath during X-ray exposure. After each compression, the radiographers asked the women to score their pain experience on a validated 11-point numerical rating scale (NRS) [22] with 0 indicating 'no pain' and 10 indicating 'unbearable pain'. We retrieved the AGD values calculated by the mammography device from the DICOM-headers. We also made video recordings ($n = 1732$) of all breast compressions for qualitative evaluation by a referent radiographer from the Dutch reference center for screening (LRCB, Nijmegen, the Netherlands).

2.3. Observer study

After the final inclusion, three breast-screening radiologists, who each have more than 9 years of experience and each have performed more than 100,000 mammogram readings, independently assessed all study images in randomized order. They were blinded for breast thickness, force, pressure, exposure settings and AGD, and they were asked to indicate for which image(s) they would require a retake in regular screening practice. If a retake was required, they had to indicate which of the following relevant ACR image quality criteria [23] were not met: breast positioning, image contrast, sharpness and/or parenchymal spreading. This observer study was performed without consensus reading.

2.4. Statistical analysis

To compare the differences between pressure-standardized and force-standardized compressions, five outcome measures were defined: (a) the average compressed breast thickness; (b) average glandular dose; (c) average pain score; (d) the proportion of women experiencing severe pain ($NRS \geq 7$), and; (e) the proportion of images for which one or more radiologists required a retake as part of the observer study. Based on Lilliefors tests

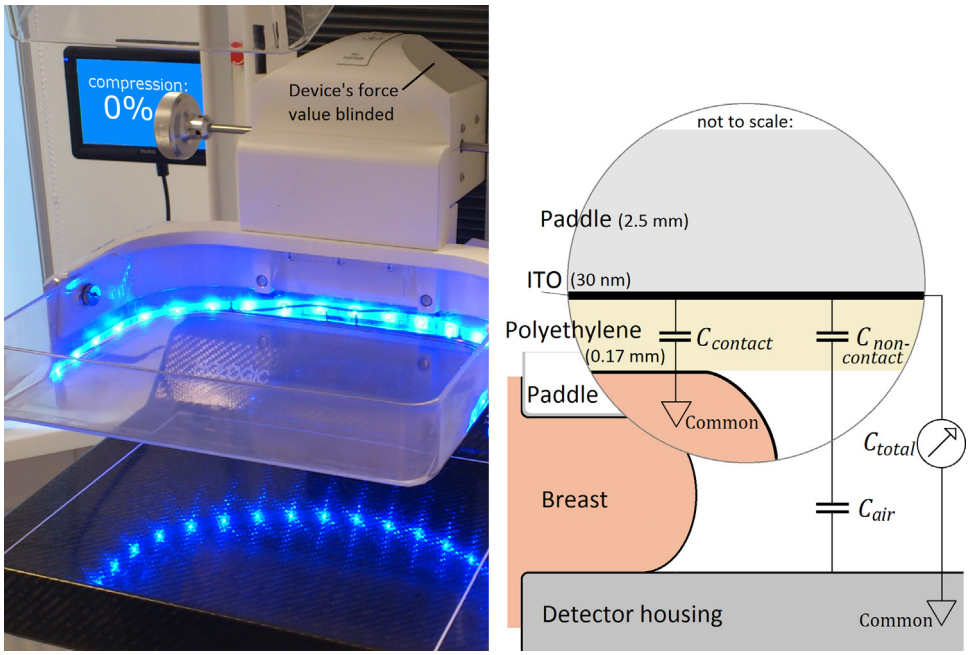

Fig. 1. Modifications to the mammography device. Left: paddle and custom display (top left) showing the compression level as percentage of the blinded target force or pressure. Right: electrical model of the contact area detector (see description in Appendix A).

for normality, Wilcoxon signed-rank tests were used for assessing the statistical significance of the differences in thickness, AGD and pain score, as well as force, pressure and contact area. Chi-squared tests were used to assess statistical significance of the differences in the proportions of women experiencing severe pain and the proportions of images requiring a retake. Diagnostic image quality of the pressure-standardized protocol was considered as good as that of the force-standardized protocol if the proportion of required retakes for pressure-standardized compressions would remain within the 95% confidence interval of the proportion for force-standardized compressions. Analyses and tests were performed with statistical software (R version 3.1, R Foundation for Statistical Computing, Vienna, Austria). Test outcomes were considered statistically significant at the $p < 0.05$ level.

3. Results

3.1. Under-compression issue and solution

During the evaluation of phase 1, the referent radiographer identified a particular compression issue from studying the available video recordings: at the beginning of a compression, e.g. at 2 daN of force, the contact area of some breasts consisted only of a small roll of skin, e.g. 0.20 dm^2. Since 2 daN divided by 0.20 dm^2 mathematically equals 10 kPa, the compression level was displayed as 100% and the image was taken, in agreement with the study protocol. However, in several of these video recordings, we noted that the breast itself was barely compressed because it was not yet in contact with the paddle. An example is shown in Fig. 2.

From studying the video recordings of the contralateral force-standardized compressions we learned that the contact area increases when the compression is continued, and that the 10 kPa target pressure is reached again but at a higher force, e.g. 8 daN/0.8 dm^2. Based on this understanding, we implemented the aforementioned two measures in the second phase (6 daN minimum force and extra radiographer training). Since the issue did not occur in phase 2, we decided to separate the results of phase 1 into two groups: the 49 cases that received forces below 5 daN for the pressure-standardized compression, and the 165 cases that received 5 daN or more. This 5 daN cutoff value for phase 1 (pressure-standardized CC-compressions) corresponds to the implemented minimum force of 6 daN for phase 2 (pressure-standardized MLO-compressions) because the ratio of average CC and MLO contact areas is approximately 5–6.

3.2. Mechanical standardization

Fig. 3 shows the applied forces plotted against contact area. The trendlines for the force-standardized protocol are predominantly horizontal, indicating that breasts of all sizes received a similar force: 14 daN. The trendlines for the pressure-standardized protocol show that the applied forces are proportional to the contact area: they follow the black dotted line which has a slope of 10 daN/dm^2, which equals 10 kPa. Both protocols were executed with high accuracy and precision: the average applied forces and pressures were 96% and 99% of their targets for CC and MLO respectively, and the standard deviations were 7.2% and 10% for force and pressure respectively. These standard deviations are much lower than the 20% standard deviation found in a typical dataset from Dutch screening [15] [“this issue”].

3.3. Differences in thickness, dose and pain

Table 1 shows the averages and standard deviations for compressed breast thickness, average glandular dose and pain scores, as well as the proportions of women experiencing severe pain (NRS ≥ 7). Compressed breast thickness is higher in the pressure-standardized compressions compared to force-standardized compressions; on average 20% (CC, force < 5 daN), 6.3% (CC, force ≥ 5 daN) and 4.2% (MLO). The average AGD values obtained from the DICOM-headers are lower for the pressure-standardized compressions: 0.6% (CC, force < 5 daN), 3.2% (CC, force ≥ 5 daN), and 0.5% (MLO). Further DICOM-header analysis revealed that the contradiction in decreased AGD for increased breast thickness could be explained by the mammography device's

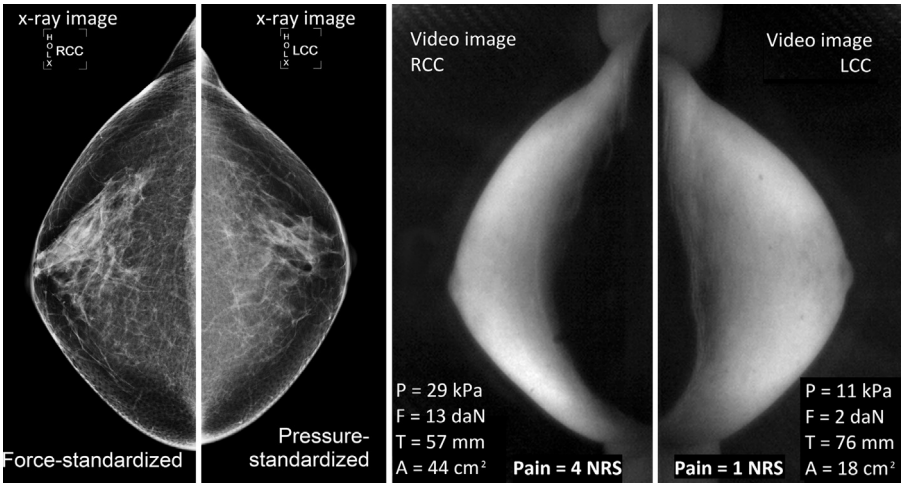

Fig. 2. Example of under-compression: left panels: X-ray images with exceptional contrast difference in the pressure-standardized compression (LCC). Right panels: corresponding visual images of the compressed breast (from video-camera positioned above the compression paddle). The contact area (shadow area on the breast) is much smaller in the pressure-standardized compression (rightmost panel).

switching of filter material (Molybdenum up to 64 mm breast thickness and Rhodium above). For the subset of 335 compression-pairs that were obtained with the same filter in both the force- and pressure-standardized compression, the AGD increase was 0.09% for an average thickness increase of 5.3%.

The average pain scores for the pressure-standardized compressions are lower than those scored for the contralateral force-standardized compressions by 46% (CC, force < 5 daN), 17% (CC, force ≥ 5 daN) and 10% (MLO). For the proportions of women reporting severe pain scores we find reductions of 86% (CC, force < 5 daN), 32% (CC, force ≥ 5 daN) and 27% (MLO). All differences are statistically significant ($p < 0.05$), except the AGD differences for MLO and CC-compressions below 5 daN. In the complementary set of force-standardized control compressions, i.e. comparing the same protocol applied to left breasts versus right breasts, none of the differences is significant (data not shown).

Fig. 4 shows compressed thickness, average glandular dose and pain score versus contact area. The 49 cases with pressure-standardized forces below 5 daN are shown separately, and illustrate that these had very small contact areas. We observe that the trendlines for dose are very similar regardless which protocol was used and despite the fact that the trendlines for thickness are distinctly different for the two protocols. In the thickness and pain panels, the trendlines for the force-protocol and pressure-protocol cross each other at contact areas of approximately 1.4 dm^2. This also applies to the trendlines in Fig. 3 and it corresponds with theory because 10 kPa = 14 daN/1.4 dm^2. In other words: for breasts with a contact area of 1.4 dm^2, these two protocols correspond to the same level of compression, which should, and did, yield the same thickness, AGD and pain score. Since 82% ($n = 353/433$) of the women had contact areas smaller than 1.4 dm^2, the pressure-standardized protocol is on average less painful than the force-standardized protocol, in particular for the 49 women who received less than 5 daN of force. Table 2 shows the proportions of women, with breast contact areas, for whom the pressure-standardized compression was more, equal or less painful than the contralateral force-standardized compression. We note that women with smaller breasts are more likely to consider the pressure-standardized method less painful.

3.4. Differences in retake proportion

Table 3 shows that the retake-proportion for the pressure-standardized CC-compressions in phase 1 is 18% ($n = 9/49$) for the cases that received less than 5 daN, and 4.2% ($n = 7/165$) for the cases that received 5 daN or higher. The latter falls within the 95% confidence interval of the retake-proportion for force-standardized CC-compressions: [0.4–4.4%] ($n = 3/214$). The proportions of retakes for phase 2 are practically the same: 16.0% ($n = 35/219$) for the pressure-standardized protocol, and 16.4% ($n = 36/219$) for the

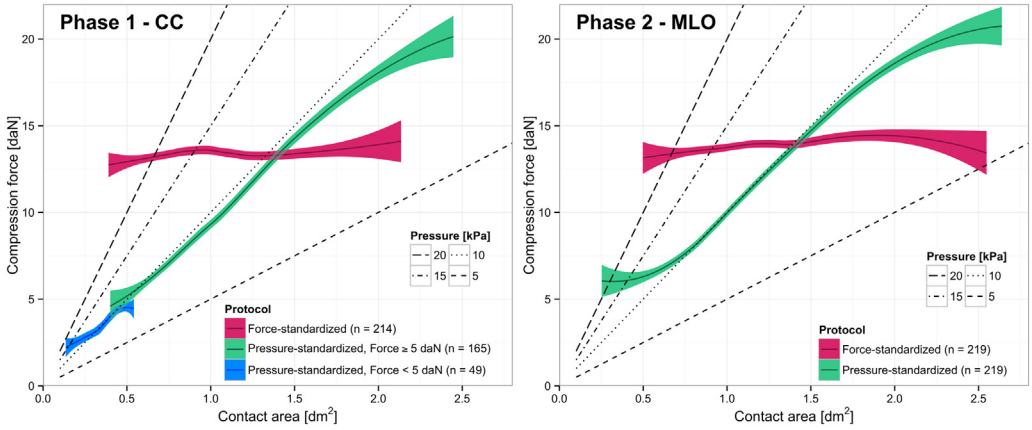

Fig. 3. Applied force versus contact area. Colored lines are local regression fit curves with 95% confidence interval: force-standardized compressions have a similar force, pressures-standardized compressions have forces that are proportional to contact area. Black lines denote equal pressures.

Table 1
Parameter values, relative differences and statistical test *p*-values for comparing the compression protocols. Abbreviations: s-r test, signed ranks test; s.d., standard deviation; n.s., not significant.

	Phase 1–CC compressions							
	Forces < 5 daN (n = 49)				Forces ≥ 5 daN (n = 165)			
	Pressure-standardized, mean ± s.d.	Force-standardized, mean ± s.d.	Relative difference [%]	Wilcoxon s-r test, p-value	Pressure-standardized, mean ± s.d.	Force-standardized, mean ± s.d.	Relative difference [%]	Wilcoxon s-r test, p-value
Contact pressure [kPa]	9.67 ± 1.26	21.3 ± 5.20	−55	<.001	9.48 ± 0.90	13.1 ± 3.92	−28	<.001
Compression force [daN]	3.70 ± 0.89	13.2 ± 0.84	−72	<.001	9.62 ± 3.67	13.4 ± 1.04	−28	<.001
Contact area [dm^2]	0.37 ± 0.11	0.65 ± 0.16	−43	<.001	1.02 ± 0.40	1.11 ± 0.32	−8.1	<.001
Compressed thickness [mm]	73.5 ± 13.2	61.2 ± 12.6	20	<.001	65.7 ± 10.6	61.8 ± 9.8	6.3	<.001
Average glandular dose [mGy]	1.75 ± 0.45	1.76 ± 0.41	−0.6	n.s.	1.84 ± 0.40	1.92 ± 0.43	−4.2	<.001
Pain after mammogram [NRS]	2.96 ± 2.31	5.51 ± 2.49	−46	<.001	4.29 ± 2.57	5.14 ± 2.57	−17	<.001
	Proportion	Proportion	Relative difference [%]	χ^2 test	Proportion	Proportion	Relative difference [%]	χ^2 test
Severe pain (NRS ≥ 7)	.061 (n = 3)	.429 (n = 21)	−86	<.001	.236 (n = 39)	.345 (n = 57)	−32	.04

	Phase 2—MLO compressions Forces ≥ 6 daN (all, n = 219)			
	Pressure-standardized, mean ± s.d.	Force-standardized, mean ± s.d.		Wilcoxon s-r test, p-value
Contact pressure [kPa]	9.97 ± 0.99	12.6 ± 3.57	−21%	<.001
Compression force [daN]	11.1 ± 3.99	13.9 ± 0.97	−20%	<.001
Contact area [dm^2]	1.12 ± 0.46	1.19 ± 0.36	−5.9%	<.001
Compressed thickness [mm]	68.7 ± 10.7	65.9 ± 10.8	4.2%	<.001
Average glandular dose [mGy]	2.13 ± 0.52	2.14 ± 0.53	−0.5%	n.s.
Pain after mammogram [NRS]	4.71 ± 2.40	5.23 ± 2.56	−9.9%	<.001
	Proportion	Proportion	Relative difference	χ^2 test
Severe pain (NRS ≥ 7)	.256 (n = 56)	.352 (n = 77)	−27%	.04

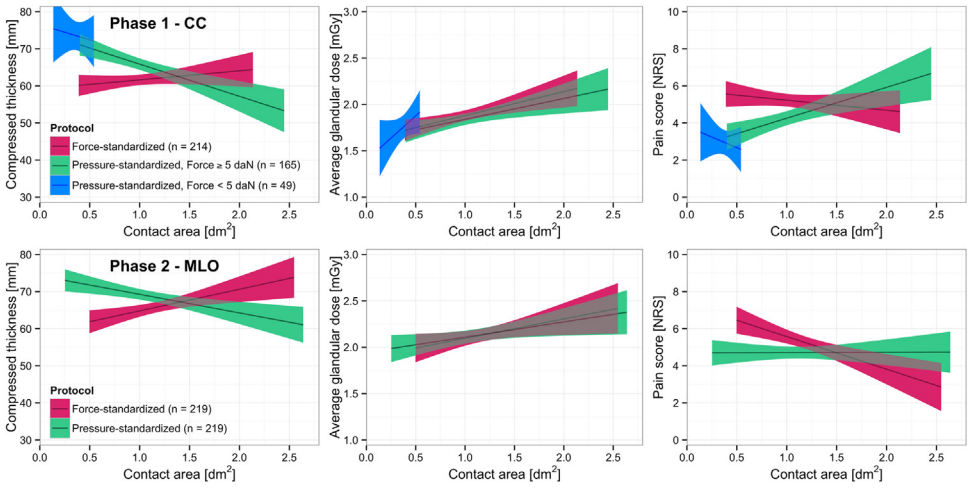

Fig. 4. Compressed breast thickness, average glandular dose and pain score versus contact area. Colored lines are linear regression fit curves with 95% confidence interval: For smaller breasts, the pressure-standardized protocol leads to higher compressed thickness. There is no difference for the AGD. The pain scores are significantly lower for small breasts (less pronounced for MLO).

Table 2
Which women experienced more, equal or less pain with the pressure-standardized compression? Abbreviations: pctl, percentile.

	Phase 1–CC compressions				Phase 2–MLO compressions	
	Forces < 5 daN (n = 49)		Forces ≥ 5 daN (n = 165)		Forces ≥ 6 daN (all, n = 219)	
	Proportion	Contact area [dm^2] Mean [5th–95th pctl]	Proportion	Contact area [dm^2] Mean [5th–95th pctl]	Proportion	Contact area [dm^2] Mean [5th–95th pctl]
More pain	.02 (n = 1)	0.51 [N/A for n = 1]	.14 (n = 23)	1.34 [0.79–1.98]	.16 (n = 35)	1.40 [0.78–2.13]
Equal pain	.14 (n = 7)	0.55 [0.35–0.66]	.36 (n = 59)	1.15 [0.71–1.71]	.38 (n = 83)	1.23 [0.69–1.93]
Less pain	.84 (n = 41)	0.51 [0.32–0.67]	.50 (n = 83)	0.93 [0.59–1.39]	.46 (n = 101)	1.01 [0.58–1.49]

Table 3
Numbers of retakes required by one or more radiologists from the observer study and the reason(s) given.

	Number of retakes	One or more reason(s) for retakes (ACR criteria)			
		Positioning	Contrast	Sharpness	Spreading
Phase 1 – CC compressions					
Pressure-standardized, forces < 5 daN (n = 49)	9	7	2	1	0
Pressure-standardized, forces ≥ 5 daN (n = 165)	7	6	1	0	0
Force-standardized (n = 214)	3	3	0	0	0
Phase 2 – MLO compressions					
Pressure-standardized (n = 219)	35	35	0	1	0
Force-standardized (n = 219)	36	36	1	0	0
Force-standardized controls					
CC compressions from phase 2 (n = 438)	9	9	0	0	0
MLO compressions from phase 1 (n = 414)	43	43	0	0	0
Total	142	139	4	2	0

force-standardized protocol, which has a 95% confidence interval of [11.9–22.2%].

In general, more retakes were required for MLO-compressions than for CC-compressions. This applies both to the pairs of pressure- and force-standardized compressions and to the control compressions (Table 2). 98% (n = 139/142) of the retakes were ascribed to sub-optimal breast positioning, regardless of which protocol was used. There were no recalls from home, neither by the radiologists of the observer study, nor by the radiologists of the regular screening process.

4. Discussion

In this study we have implemented a 10 kPa pressure-standardized mammographic compression protocol, which was intra-individually compared with a 14 daN force-standardized protocol. The essential difference is that in the pressure-standardized protocol, the applied force is proportional to the size of the breast (contact area), whereas in the force-standardized protocol, the same force is applied to each breast. Compared with the force-standardized protocol, where pressures up to 33 kPa (ca. 250 mmHg) were reached, the pressure-standardized protocol resulted in a pressure reduction for the majority of participants. As a consequence, average pain and especially the occurrence of severe pain were significantly lower in the pressure-standardized protocol: about half the participants reported less pain and around one third reported no difference. The proportion of retakes for women who received 5 daN or higher were similar, a counter-intuitive AGD reduction has been explained, and an under-compression issue in phase 1 was effectively solved with two simple measures in phase 2. All this suggests that a pressure-standardized protocol with a 10 kPa target pressure could be used in practice.

4.1. Under-compression

A breast could be called under-compressed when additional force would have reduced AGD and/or improved lesion conspicuity. An example due to insufficient compression is shown in Fig. 2. At the evaluation of phase 1, we learned from the radiographers that they trusted the displayed percentage of the compression level, but that they had to look away from the breast in order to see the display. We could not change the position of the display during this study. Instead, we implemented a minimum force and instructed the radiographers to continue the compression to a pressure of 10 kPa in which the contact area involves the actual breast. For clinical implementation, a minimum force may not be necessary if the pressure value display, or other indicator, is positioned closer to the breast so that it is in the field of view of the radiographer.

In literature we found two other effects that could contribute to under-compression. First, Dustler et al. [24] suggested that part of the applied force may be lost to compressing the (harder) pectoral muscle or stretching the skin above the breast. In a hypothetical example, this may mean that a displayed force of 8 daN, which is considered sufficient in some places, may result in an effective compression force of e.g. 5 daN, for which under-compression is a realistic possibility. Second, Hogg et al. [25] studied how the height of the detector table influences the breast contact area. In our study, while watching the video recordings of the breast compressions from phase 1, the referent radiographer frequently remarked that the detector table was positioned too low. These insights were shared with the radiographers during the extra training before phase 2.

4.2. Over-compression

A breast could be called over-compressed when additional force did not reduce AGD and/or improve image quality. The example in Fig. 5 can be considered such a case because the pressure-standardized compression required less than half of the force applied in the force-standardized compression, while AGD differed only 7% and no differences in image quality were observed.

In the 90s, concern was expressed [26] that breast compression might cause tumor cell shedding into the circulatory system. A recent pilot study by Förnvik et al. [27], examining the pressure distributions during mammographic compression of known lesions, found no such evidence. However, over-compression is still a cause of unnecessary pain.

4.3. Optimal compression?

Despite the colloquial use of the term “breast compression”, breast tissues are technically incompressible. The purpose of applying force is to spread the tissue and make the breast flatter. Under external loading, the breast follows a deformation that is characteristic for incompressible viscoelastic materials [28]. This suggests that there are two processes involved: viscous effusion of liquids [blood and lymph], and elastic deformation of soft tissues [adipose, glandular, ligaments, skin]. For this study, we chose a target pressure of 10 kPa (75 mmHg) because it is expected to result in a tissue pressure between normal venous and arterial blood pressure. The aim is that most of the blood (the venous compartment) is evacuated from the breast. This effectively reduces the breast volume, which is one way to achieve thickness reduction. Applying more pressure has less benefit in terms of volume reduction, but additional thickness reduction is still achieved by further tissue spreading. This may however be more painful.

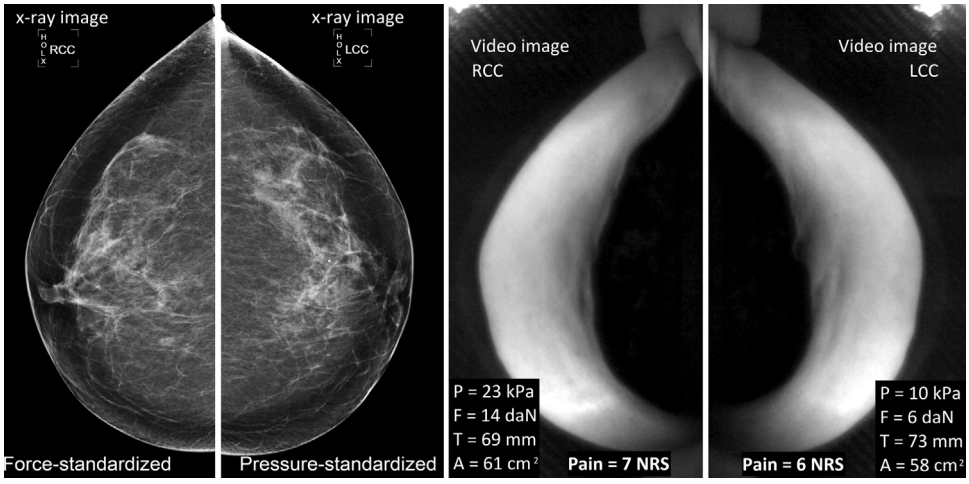

Fig. 5. Example of over-compression: Left panels: X-ray images show no observable differences despite 8 daN higher force in the force-standardized compression (RCC). Right panels: corresponding visual images of the compressed breast (from video-camera positioned above the paddle). The contact area (shadow area on the breast) is similar for the left and right breast.

4.4. Limitations

In our study, the pressure-standardized protocol required forces higher than the force-standardized protocol for 18% ($n = 80/433$) of the women because their breast contact area was larger than 1.4 dm^2. The design of our study did not allow concluding whether this additional force was beneficial for image quality or AGD. Since compressions with a 14 daN target are currently accepted in the daily practice of Dutch screening, one may consider implementing a pressure-standardized protocol with an upper force-limit to avoid unnecessary pain from over-compression.

With the aim to study whether and how mammographic breast compression can be better standardized, we compared the 10 kPa pressure-standardized protocol to a strict implementation of the target force of 14 daN used in Dutch screening. For performing a controlled and blinded study, we only showed the compression level as percentage of the target values. This way of working is not representative for conventional daily practice [15] ["this issue"], and therefore represents a limitation. However, as a result of this blinding, the standard deviation in applied forces and pressures was much lower than in normal practice, which means that standardization was improved by decreasing radiographer variability [16].

Although the sample size of this study provided sufficient statistical power to draw conclusions for screening-participants, we did not encounter enough cases for comparing the conspicuity of lesions between the two compression protocols. This remains a subject for further studies.

5. Conclusion

We have shown that, with minimal extra radiographer training, it is possible to implement pressure-standardized compression to a specific target pressure, in this case 10 kPa. From intra-individual comparison with a 14 daN target force-standardized protocol, as implemented in the Dutch screening, we conclude that, for the majority of women, pressure-standardized compression reduces pain, especially severe pain, without compromising image quality. The average glandular dose and retake proportions were similar for both protocols.

5.1. Recommendation

Now that we identified and solved the challenges of pressure-standardized compression, we consider the technique ready for a study in which two groups of women randomly receive *all* breast compressions either force- or pressure-standardized in the first screening round and switching protocols for the second round (2 years later). Such a randomized control crossover trial should give accurate outcomes with a view to clinical implementation.

Conflict of interest

W. Branderhorst is an employee at Sigmascreening. C.A. Grimbergen is an employee, founder, board member, and patent holder of Sigmascreening. G.J. den Heeten is a founder of Sigmascreening and co-patent holder on behalf of the Academic Medical Center Amsterdam. J.E. de Groot and M.J.M. Broeders have no conflicts of interest to declare.

Role of the funding source

The funding source had no involvement in the conduction of the research or preparation of the manuscript.

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Appendix A.

A.1. Capacitive contact area sensor

We measured the contact area between the breast and the compression paddle using a capacitive sensor [29] design as illustrated in Fig. 1b. We covered the entire bottom surface of the used paddles with a 0.17 mm thin polyethylene sheet of which the surface facing the paddle was homogeneously coated with 30 nm of electrically conducting indium tin oxide (ITO). Breast visibility and X-ray image quality are maintained due to the sheet's optical transparency, homogeneity, and more than 99.5% transparency in the

used X-ray spectra. When the breast is positioned on the electrically conducting surface of the electrically common (grounded) carbon composite detector housing, the theoretical capacitance C_{total} with respect to the ITO layer has a dependency on contact area ($C_{contact}$ and the complementary $C_{non\text{-}contact}$), and on breast thickness (i.e. the air gap: C_{air}). However, since even the thinnest breast (assumed 25 mm) is much thicker than the 0.17 mm polyethylene sheet, the thickness dependency is about 40 times weaker and can be neglected. Empirically we measure:

$$C_{total} \approx C_p + f \cdot A \quad \text{(A1)}$$

in which C_p is a constant parasitic capacitance of the electric circuit, and the factor f relates the measured capacitance value to the actual breast contact area A. Both values were calibrated and remained within 3% inaccuracy for all occurring breast contact areas $A \leq 3\,dm^2$ and thicknesses ≥ 25 mm.

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