Title: Comparison of screening performance metrics and patient dose of two mammographic image acquisition modes in the Danish National Breast Cancer Screening Programme

Authors: Ahmed Jibril Abdi, Andreas Fieselmann, Heiderose Pfaff, Thomas Mertelmeier, Lisbet Brønsø Larsen

PII: S0720-048X(18)30215-8
DOI: https://doi.org/10.1016/j.ejrad.2018.06.010
Reference: EURR 8220

To appear in: European Journal of Radiology

Received date: 21-2-2018
Revised date: 9-6-2018
Accepted date: 14-6-2018

Please cite this article as: Abdi AJ, Fieselmann A, Pfaff H, Mertelmeier T, Larsen LB, Comparison of screening performance metrics and patient dose of two mammographic image acquisition modes in the Danish National Breast Cancer Screening Programme, European Journal of Radiology (2018), https://doi.org/10.1016/j.ejrad.2018.06.010

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
Comparison of screening performance metrics and patient dose of two mammographic image acquisition modes in the Danish National Breast Cancer Screening Programme

All Authors:
Ahmed Jibril Abdi
Andreas Fieselmann
Heiderose Pfaff
Thomas Mertelmeier
Lisbet Brønsro Larsen

1Clinical Engineering Department, Region of Southern Denmark, Area of diagnostic Radiology, J. B. Winsløws Vej 4, 5000 Odense C, ved indgang 34, 5000 Odense C, E-mail: ahmed.abdi@rsyd.dk, Phone: +45 20422535
2Siemens Healthcare GmbH, Forchheim, Germany
3Odense University Hospital, Mammography Section, Radiology Department, Sdr. Boulevard 29, 5000 Odense C, Denmark

*Corresponding author:
Ahmed Jibril Abdi
1Clinical Engineering Department, Region of Southern Denmark, Area of diagnostic Radiology, J. B. Winsløws Vej 4, 5000 Odense C, ved indgang 34, 5000 Odense C, E-mail: ahmed.abdi@rsyd.dk, Phone: +45 20422535

Abstract

Introduction: In this study, screening performance metrics and radiation dose were compared for two image acquisition modes for breast cancer screening with MAMMOMAT Inspiration (Siemens Healthcare GmbH, Forchheim, Germany). This mammography system can operate without an anti-scatter grid in place but using software scatter correction instead. This grid-less acquisition mode (PRIME) requires less patient dose due to the increase in primary radiation reaching the detector. This study retrospectively analyses data from the Region of Southern Denmark where the grid-less mode has been installed in November 2013 and replaced grid-based screening.

Methods and materials: A total of 72,188 screening cases from the same geographical region in Denmark were included in the study. They were subdivided into two study populations: cases acquired before and after installation of the grid-less acquisition mode. Sensitivity and specificity of breast cancer screening were calculated for the two populations; thus representing the performance of grid-less and grid-based screening. To measure the entrance surface air kerma (ESAK) additional phantom tests were carried out.
Polymethylmethacrylate (PMMA) attenuation plates with different thicknesses (20-70mm in steps of 10mm) simulated the compressed breast (21mm-90mm) and a solid-state dosimeter was used.

**Results:** Statistical testing of the results showed that screening with grid-less acquisition provides equivalent performance with respect to sensitivity and specificity compared to grid-based screening. The specificity was 98.11% (95% confidence interval (CI) from 97.93% to 98.29%) and 97.96% (95% CI from 97.84% to 98.09%) for screening with grid-less acquisition and grid-based acquisition, respectively. The cancer detection rate as a measure for sensitivity was equal (0.55%) for grid-less screening and grid-based screening. An average glandular dose saving between 13.5% and 36.4% depending on breast thickness in grid-less acquisition was obtained compared to grid-based acquisition.

**Conclusion:** Statistically significant equivalence was shown with an equivalence margin of 0.12 percentage points for cancer detection rate and with an equivalence margin of 0.40 percentage points for specificity. A marked patient dose savings in grid-less acquisition of up to 36% compared to grid-based acquisition was achieved. It can be concluded that grid-less acquisition with software scatter correction is an alternative to grid-based acquisition in mammography.
Introduction

To acquire images with low patient dose is of high importance in screening mammography where asymptomatic women are examined. At the same time mammographic image quality must be high to have high sensitivity and specificity during breast cancer screening. The ALARA (as low as reasonable achievable) principle states that patient dose should be low however image quality and diagnostic performance must not be compromised. Over the last years, several technical approaches have been developed that allow reducing patient dose while keeping image quality at a high level.

One example is the optimisation of beam spectra for digital mammography [1]. Another method for dose reduction is lowering patient dose and employing noise reduction to mitigate effects of quantum noise in the image. Noise reduction in clinical breast images is an important issue in order to distinguish the small cancer tumours and micro-calcifications. Computational denoising techniques may reduce both noise on the clinical image and radiation exposure to the patient in both full field digital mammography (FFDMG) and digital breast tomosynthesis (DBT) [2–4].

A further example is acquiring digital mammography images without hardware anti-scatter grid but using a software solution to mitigate the scattered X-ray radiation [5]. The anti-scatter grid also attenuates a certain amount of the primary (non-scattered) radiation. When the anti-scatter grid is removed more primary radiation can reach the detector. It has been shown that patient dose can be reduced depending on the compressed breast thickness when the anti-scatter grid is removed and a software scatter correction is employed [6,7].

Besides investigating dose reduction aspects when using grid-less mammography with software scatter correction it is also very important to investigate the performance of this new mammographic acquisition technique in a screening environment. I.e. it is to investigate that the screening performance is not affected negatively when using the new method. Two important metrics of screening performance are the cancer detection rate and the non-cancer recall rate.

In our study, we retrospectively analyse data from the Danish National Breast Cancer Screening Programme in which images have been acquired in the same geographical region with the conventional imaging method (with grid) and the new acquisition method (without grid and software scatter correction). We compare cancer detection rate and the non-cancer recall rate between the two acquisition modes. To assess patient dose phantom dose measurements were conducted.
Methods and Materials

1.1 Danish national screening programme
A national breast cancer screening programme was implemented in Denmark in 2007 [8,9]. Women aged 50 to 69 years are offered a screening mammogram free of charge every two years. Denmark consists of the following five Regions which have their own booking systems and send personal invitations to the women.

- Capital Region Denmark (Hovedstaden)
- Region Zealand (Sjælland)
- North Denmark Region (Nordjylland)
- Central Denmark Region (Midtjylland)
- Region of Southern Denmark (Syddanmark)

Participation rate in the screening programme is 65% to 82% depending on the Region and the mean age of women who participate in screening is 59 years [8]. Two images of each breast are acquired at each screening session. All images are read independently by two radiologists and at least one of them is an experienced breast screening radiologist [8]. For quality control, the radiation dose should be measured once a week on all technical equipment used for mammography screening [8].

Quality indicators from the screening programme are collected and stored in the Danish Quality Database of Mammography Screening (Dansk Kvalitetsdatabase for Brystkræftscreening, DKMS). There are three organisational (participation, screening interval, time to result) and eight clinical (recall rate, relative number of interval cancers, relative number of invasive tumors, relative number of node negative cancers, relative number of small cancers, number of women with breast conserving therapy, ratio of surgery for benign versus malignant lesions) quality indicators.

1.2 Grid-less imaging with software scatter correction (PRIME)
All mammography systems in the Region of Southern Denmark (MAMMOMAT Inspiration, Siemens Healthcare GmbH, Forchheim, Germany) were upgraded between November 11, 2013 and November 21, 2013 to allow acquiring images without anti-scatter grid and with software scatter correction for breasts with a compressed thickness of up to 69 mm.

This acquisition mode is denoted as PRIME (Progressive Reconstruction Intelligently Minimising Exposure; not commercially available in all countries) acquisition mode. The scatter correction algorithm receives an input image which contains both primary and scattered radiation. The algorithm identifies the scatter field image in the input image. The scatter field image is then subtracted from the input image and thus the output image contains only breast tissue structures [7]. The functionality of this algorithm is illustrated in Figure 1.
A current limitation of the scatter correction algorithm is that it cannot be used when a breast implant is visible in the acquired image. Another limitation is that the detector dose increases when not using an anti-scatter grid. To avoid saturation of the pixel values in the image the PRIME acquisition mode is currently limited to breasts with a compressed thickness of up to 69mm.

1.3 Comparison of Screening Performance Metrics

1.3.1 Study Populations
To compare screening performance of the two mammographic image acquisition modes (conventional acquisition and grid-less acquisition (PRIME mode) we compare data collected from December 01, 2013 to April 30, 2014 (5 months after PRIME has been installed) with data collected from January 01, 2012 to December 31, 2012 (12 months before PRIME has been installed) in the Region of Southern Denmark. The populations are denoted as A and B.

- Population A: after installation of PRIME feature, 22,117 women screened
- Population B: before installation of PRIME feature (reference population), 50,071 women screened

Because both populations come from the same screening region, the characteristics of these populations can be considered to be equivalent. No patient-specific information was processed and this study did not require ethics committee approval.

1.3.2 Screening performance metrics
Sensitivity and specificity are common performance metrics of a screening method. For our following analyses, the specificity of breast cancer screening is estimated as:

\[ \text{Specificity} \approx 1 - \text{NCRR} \]  \hspace{1cm} (2)

where NCRR means non-cancer recall rate (that is equivalent to the false positive rate) and is defined as:

\[ \text{NCRR} = \frac{\text{NWR} - \text{NWC}}{\text{NWS}} \]  \hspace{1cm} (3)

NWR is number of women recalled, NWC is number of women with screen-detected cancer and NWS is number of women screened. In breast cancer screening, the sensitivity of a screening method cannot be determined in absolute numbers because the cancer prevalence rate (CPR) in a screening population is not known exactly. Assuming that the two study populations described in section 1.3.1. have the same CPR one can measure the sensitivity difference based on the two cancer detection rates as:

\[ \text{Sensitivity difference} = \frac{\text{CDR}_1 - \text{CDR}_2}{\text{CPR}} \]  \hspace{1cm} (4)
where CDR1 is cancer detection rate 1, CDR2 is cancer detection rate 2 and CPR is cancer prevalence rate. The difference of the cancer detection rates is proportional to the sensitivity difference and will be used as a measure to evaluate the equivalence of the sensitivity of the two screening methods.

1.3.3 Hypothesis testing
The aim of this study is to test for equivalence of the specificity and sensitivity of the two acquisition methods. The testing is performed using the principle of confidence interval inclusion. I.e., the 100(1-2α)% confidence interval of the difference of the specificities of the two populations must be inside a given range. α is the significant level.

The difference of the cancer detection rates, which is proportional to the sensitivity difference, is also tested using this principle. The null hypothesis $H_{0,SP}$ and the alternative hypothesis $H_{1,SP}$ for testing for equivalence of the specificity in population A ($SP_A$) and the specificity in population B ($SP_B$) are:

$$H_{0,SP}: |SP_A - SP_B| > \delta_{SP}$$
$$H_{1,SP}: |SP_A - SP_B| \leq \delta_{SP}$$

The null hypothesis $H_{0,CDR}$ and the alternative hypothesis $H_{1,CDR}$ for testing for equivalence of the cancer detection rates in population A ($CDR_A$) and the cancer detection rate in population B ($CDR_B$) are:

$$H_{0,CDR}: |CDR_A - CDR_B| > \delta_{CDR}$$
$$H_{1,CDR}: |CDR_A - CDR_B| \leq \delta_{CDR}$$

The equivalence margin $\delta_{SP}$ was set to 0.40 percentage points (pp) and the equivalence margin $\delta_{CDR}$ was set to 0.12pp. The choice of these margins is explained below. No prior studies have been identified that could be used to define the equivalence margins.

Therefore, the margins were derived from the existing data from the first (2007-2010) and second (2010-2012) screening round of the five Danish regions. These data show that the specificity changed by 0.23pp ± 0.56pp (range -0.35pp to 1.04pp) from the first to the second screening round. If the value from the North Denmark Region which had the lowest number of women screened is considered to be an outlier and is neglected then the specificity, based on 4 regions, changed by 0.03pp ± 0.38pp (range -0.35pp to 0.40pp). $\delta_{SP}$ was set equal to the maximum absolute value of the range of specificity differences assuming that the obtained differences are clinically acceptable. A conservative estimate, considering the value from North Denmark as an outlier, gives $\delta_{SP}=0.40pp$.

Applying the same procedure to determine $\delta_{CDR}$ would give 0.37pp since the cancer detection rate decreased in the Region Zealand by -0.37pp from the first to the second screening round. However, since
the cancer detection rate usually decreases from the first to the second screening round, a lower margin of one third of this value was chosen which gives 0.12pp. In order to account for multiple testing a Bonferroni correction was applied. With a significance level of $\alpha=0.05$ this leads to $100(1-2(\alpha/2))\%=95\%$ confidence intervals being evaluated for the specificity difference and the cancer detection rate difference, respectively. All analyses were performed using the R statistics software version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

1.4 Phantom Measurement

1.4.1 Dose Measurement

In the Danish Quality Database of Mammography Screening the individual patient dose values are not reported [8]. To compare patient dose values between the two acquisition modes phantom dose measurements were carried out. Mammography systems provide clinical dose indications as entrance surface air kerma (ESAK) and average glandular dose (AGD). The technical measurement allows for more accurate dose measurement for all possible breast thicknesses. Therefore, the standard technical dose measurement described in the technical literatures and in the European guidelines for quality assurance in breast cancer screening and diagnosis was used in this study [10,11].

PMMA attenuation plates with different thicknesses (20-70 mm in steps of 10mm) were used to simulate compressed breast thicknesses corresponding to 21mm to 90mm (Table 3).

A Black Piranha 657 (RTI Electronics AB, Mölndal, Sweden) solid-state dosimeter was used to measure the dose. To measure the ESAK, the PMMA plates were placed on the breast support (Bucky) of the system as shown in Figure 2. The MAMMOMAT Inspiration mammography system was set in automatic exposure control (AEC) mode, where exposure parameters including target/filter combination and tube current (mAs) were generated automatically. All thickness of PMMA attenuation plates (from 20-70 mm in steps of 10 mm) were exposed using the AEC mode to simulated equivalent compressed breast tissue thicknesses (21 to 90mm). All generated exposure parameters were then noted in a spreadsheet (Table 7). The AEC was then deactivated, the solid-sate dosimeter was placed on the top of the PMMA plates and the exposure was measured using manual input of the recorded parameters from the AEC mode (see Figure 3). The average glandular dose (AGD) was calculated according to equation 9 [12,13].

$$\text{AGD} = K \cdot g \cdot c \cdot s$$

(9)

$K$ is the incident air kerma measured by the dosimeter. $g$, $c$ and $s$ are factors taking into account the conversion from input air kerma to glandular dose, the correction for glandularity, and the target filter combination. The relationship between PMMA thickness and breast tissue glandularity, which is shown in Table 3 was used to compute the AGD.
2.4.2 Contrast to noise ratio assessment
The contrast-to-noise ratio (CNR) of both grid-less and grid-based acquisition was assessed. To determine
the CNR a contrast object of 50mm x 50mm x 0.2mm aluminium foil was placed on the top of PMMA plates
for all PMMA thicknesses. CNR was calculated using the equation 10 [14]:

\[
\text{CNR} = \frac{|\text{ROI}_{\text{Al}} - \text{ROI}_{\text{PMMA}}|}{\sqrt{\text{SD}_{\text{Al}}^2 + \text{SD}_{\text{PMMA}}^2}} \quad (10)
\]

where ROI\text{Al} is the region of interest’s mean pixel value of the test object (aluminium foil) and ROI\text{PMMA} is the
region of interest’s mean pixel value of the PMMA block. The SD\text{Al} and SD\text{PMMA} are the standard deviation of
the pixel values in the regions of interest of the test object and PMMA block respectively.

Results
1.5 Comparison of Screening Performance Metrics
The number of women screened, the number of women recalled and the number of women with cancer
are shown in Table 4 for each of the two populations. The recall rate, cancer detection rate and specificity
as well as their 95% confidence intervals that were computed from the data in Table 4 are shown in Table
5. The differences of the recall rate, cancer detection rate and specificity between population A and B
including the 95% confidence intervals that were computed from the data in Table 4 are shown in Table 6.

The difference of the cancer detection rates of the two screening methods - which is proportional to the
sensitivity difference - is 0.00pp, i.e. both methods achieved the same cancer detection rates. The 95%
confidence interval of the difference (-0.12pp to 0.11 pp) is included in the equivalence interval for the
cancer detection rate (-0.12pp to 0.12pp). Therefore, statistically significant equality of the cancer
detection rates can be shown.

Grid-less acquisition resulted in a slightly higher specificity compared to grid-based screening (difference
0.15pp). The specificity values were 98.11% (95% CI from 97.93% to 98.29%) and 97.96% (95% CI from
97.84% to 98.09%) for screening with the grid-less feature and grid-based screening, respectively. The 95%
confidence interval of the difference (-0.07pp to 0.36pp) is included in the equivalence interval of the
specificity (-0.40pp to 0.40pp). Therefore, also statistically significant equality of the specificities can be
shown.

The sensitivity was evaluated based on the difference of cancer detection rates which is proportional to the
sensitivity difference. The cancer detection rates were 0.55% (95% CI from 0.45% to 0.64%) and 0.55% (95%
CI from 0.49% to 0.62%) for screening with the PRIME feature and grid-based screening, respectively. Statistically significant equivalence was shown with an equivalence margin of 0.12 percentage points.

1.6 Dose measurement

The measured half value layer (HVL), ESAK and other relevant parameters of both grid-based X-ray mammography acquisition and PRIME (grid-less) acquisition are summarised in Table 7. The difference between the ESAK of PRIME (grid-less) mammography acquisition and grid-based mammography acquisition are also shown in this table. The calculated AGD for all breast tissue thicknesses are presented in Table 8 including the difference between the calculated AGD of PRIME (grid-less) and grid-based mammography acquisitions. Patient dose savings in grid-less acquisition (PRIME) range between 13.5% and 36.4% compared to grid-based acquisition. The graphical comparison between the calculated AGD of grid-based and grid-less (PRIME) is shown in Figure 4.

1.7 Contrast-to-noise ratio (CNR)

The calculated CNR is similar for the grid-less and grid based acquisition. A graphical comparison of CNR as a function of increasing equivalent breast thickness is shown in Figure 5. The calculated p-value of correlation between the CNR of grid-less and grid-based acquisition is p= 0.000024.
**Discussion and Summary**

The study collected data from two large populations with a total of 72,188 women. The specificity values obtained in this study (97.96%, 98.11%) were similar to the data from the previous screening round (2010-2012) in the Region of South Denmark (97.98%) (Table 2). The cancer detection rates obtained in this study (0.55%, 0.55%) were slightly lower compared to the cancer detection rate from the previous screening round (2010-2012; 0.63%) in this region (Table 2).

A potential limitation of the study analysing the screening data is that two different populations were used. Although the two populations are from the same geographical region and from similar points in time there could be a different distribution of cancer cases in the populations. Additionally, the radiologists reading the images in both populations could be different. However, due to the large amount of screening cases in both populations the impact of this kind of variability is expected to be low. To investigate the dose saving factor in grid-less X-ray mammography acquisition compared with grid-based X-ray mammography acquisition, ESAK was directly measured. The measured ESAK in both grid-less mode (PRIME) and conventional X-ray mammography acquisitions obtained in this study were very close to the measured ESAK and calculated AGD results from the results obtained in a previous study[6]. However, both measured ESAK and calculated AGD obtained in this study, were slightly higher than the measured ESAK in the previous study[6].

In this phantom study, the solid-state dosimeter was placed on the PMMA attenuation plates. In the previous study, the dosimeter was placed directly on the breast support (Bucky) with a detector protective steel plate and a distance correction was used according to inverse square low to determine the correct ESAK. Moreover, a Mo/Mo filter-target combination was used in the 20 mm - 30 mm PMMA thickness range in the previous study. However, the filter-target combination used in this study was W/Rh for all PMMA thicknesses. Therefore, the measurement technique used in this study differs from the measurement technique used in the previous study, which may be the reason of this difference between dose saving factors.

The radiation dose saving factor decreases with increased compressed breast thickness because of the larger scatter fraction for thicker breasts. Therefore more primary radiation is required for compensating the noise component associated with scattered radiation. The higher benefit of grid-less acquisition can thus be found for thinner breasts where the additional primary radiation allows lowering overall patient dose to achieve the same CNR as an acquisition with grid.

In a recent study by Van Peteghem et al.[15], the patient dose data was extracted from two populations: one where PRIME was used for image acquisition, the other used traditional acquisition with anti-scatter
grid. The dose saving with PRIME obtained in the study by Van Peteghem et al. (27.7% / 15.6% / 9.9% for 20-29mm / 40-49mm / 60-69mm compressed breast thickness) is similar to the dose saving we obtained in our phantom dose measurements (36.4-21.5% / 18.3% / 16.0-14.2% for 21-32mm / 45mm / 60-75mm compressed breast thickness; Table 8).

In summary, screening performance metrics of breast cancer screening with a mammography system operating without a grid and with software scatter correction have been evaluated and results were compared to those obtained with grid-based screening. Two populations from the same geographical region in Denmark were considered in this study. The reference population (50,071 women) received grid-based screening whereas the women in the second population (22,117 women) received screening with the grid-less feature (PRIME). Recall rates and cancer detection rates were determined from the study populations and specificity of each method was computed from these data. Statistically significant equivalence was shown with an equivalence margin of 0.40 percentage points. Overall, screening in grid-less acquisition mode (PRIME) demonstrated equal sensitivity measured as the cancer detection rate difference and equal specificity compared to grid-based screening at a significance level of α=0.05.

According to the measured ESAK and calculated AGD obtained in this study, there is clear indication of patient dose saving in grid-less X-ray mammography acquisition (PRIME) compared with conventional grid-based X-ray mammography acquisition. Up to 36.4% patient dose saving was obtained in grid-less acquisition (PRIME) compared to grid-based acquisition. The patient dose reduction in grid-less acquisition decreases with breast thicknesses. Therefore, this dose reduction factor is highly dependent on the breast thicknesses. No statistically significant difference between CNR of grid-less and grid-based acquisition was found.

Conflict of Interest: None
References


Figures

Figure 1: Illustration of the functionality of PRIME algorithm [7].

Figure 2: Dose measurement set up for acquisition using AEC mode in both grid-less and conventional X-ray mammography acquisitions.
Figure 3: Measurement set-up of entrance surface air kerma in both grid-less and grid-based acquisitions. The exposure parameters were set manually; automatic exposure control mode has been disabled in this set-up.
Figure 4: Graphical comparison of calculated AGD for all breast tissue thicknesses between the grid-less and grid-based acquisitions. For better visualization sample points are connected using a smooth fit function.

Figure 5: Graphical comparison of CNR between the grid-less and grid-based acquisition. For better visualization, sample points are connected using a smooth fit function.
### Tables

<table>
<thead>
<tr>
<th>Round</th>
<th>Regions</th>
<th>Number of women screened (NWS)</th>
<th>Number of women recalled (NWR)</th>
<th>Number of women with cancer (NWC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Capital Region Denmark</td>
<td>139,987</td>
<td>3,982</td>
<td>1,235</td>
</tr>
<tr>
<td></td>
<td>Region Zealand</td>
<td>91,113</td>
<td>2,477</td>
<td>882</td>
</tr>
<tr>
<td></td>
<td>North Denmark Region</td>
<td>48,980</td>
<td>2,351</td>
<td>434</td>
</tr>
<tr>
<td></td>
<td>Central Denmark Region</td>
<td>115,717</td>
<td>2,351</td>
<td>434</td>
</tr>
<tr>
<td></td>
<td>Region of Southern Denmark</td>
<td>123,026</td>
<td>3,456</td>
<td>1,096</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>518,823</td>
<td>15,431</td>
<td>4,757</td>
</tr>
<tr>
<td>2</td>
<td>Capital Region Denmark</td>
<td>134,604</td>
<td>3,798</td>
<td>828</td>
</tr>
<tr>
<td></td>
<td>Region Zealand</td>
<td>57,640</td>
<td>1,178</td>
<td>347</td>
</tr>
<tr>
<td></td>
<td>North Denmark Region</td>
<td>61,967</td>
<td>2,150</td>
<td>369</td>
</tr>
<tr>
<td></td>
<td>Central Denmark Region</td>
<td>120,063</td>
<td>2,779</td>
<td>810</td>
</tr>
<tr>
<td></td>
<td>Region of Southern Denmark</td>
<td>127,885</td>
<td>3,387</td>
<td>810</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>502,159</td>
<td>13,302</td>
<td>3,164</td>
</tr>
</tbody>
</table>

Table 1: Number of women screened and recalled and number of women with cancer in the 5 Danish Regions in the first and second screening round.

<table>
<thead>
<tr>
<th>Round</th>
<th>Regions</th>
<th>Recall rate (NWR/NWS)</th>
<th>Cancer detection rate (NWC/NWS)</th>
<th>Specificity (1−(NWR−NWC)/NWS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Capital Region Denmark</td>
<td>2.84% (2.76-2.93)</td>
<td>0.88% (0.83-0.93)</td>
<td>98.04% (97.97-98.11)</td>
</tr>
<tr>
<td></td>
<td>Region Zealand</td>
<td>2.72% (2.61-2.82)</td>
<td>0.97% (0.90-1.03)</td>
<td>98.25% (98.16-98.33)</td>
</tr>
<tr>
<td></td>
<td>North Denmark Region</td>
<td>4.80% (4.61-4.99)</td>
<td>0.89% (0.80-0.97)</td>
<td>96.09% (95.91-96.26)</td>
</tr>
<tr>
<td></td>
<td>Central Denmark Region</td>
<td>2.99% (2.89-3.08)</td>
<td>0.95% (0.89-1.00)</td>
<td>97.96% (97.88-98.04)</td>
</tr>
<tr>
<td></td>
<td>Region of Southern Denmark</td>
<td>2.57% (2.48-2.66)</td>
<td>0.90% (0.85-0.96)</td>
<td>98.33% (98.26-98.40)</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>2.97% (2.93-3.02)</td>
<td>0.92% (0.89-0.94)</td>
<td>97.94% (97.90-97.98)</td>
</tr>
<tr>
<td>2</td>
<td>Capital Region Denmark</td>
<td>2.82% (2.73-2.91)</td>
<td>0.62% (0.57-0.66)</td>
<td>97.79% (97.72-97.87)</td>
</tr>
<tr>
<td></td>
<td>Region Zealand</td>
<td>2.04% (1.93-2.16)</td>
<td>0.60% (0.54-0.67)</td>
<td>98.56% (98.46-98.66)</td>
</tr>
<tr>
<td></td>
<td>North Denmark Region</td>
<td>3.47% (3.33-3.61)</td>
<td>0.60% (0.53-0.66)</td>
<td>97.13% (96.99-97.26)</td>
</tr>
<tr>
<td></td>
<td>Central Denmark Region</td>
<td>2.31% (2.23-2.40)</td>
<td>0.67% (0.63-0.72)</td>
<td>98.36% (98.29-98.43)</td>
</tr>
<tr>
<td></td>
<td>Region of Southern Denmark</td>
<td>0.63% (0.59-0.68)</td>
<td>2.66% (2.57-2.74)</td>
<td>97.98% (97.90-98.05)</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>2.65% (2.60-2.69)</td>
<td>0.63% (0.61-0.65)</td>
<td>97.98% (97.94-98.02)</td>
</tr>
</tbody>
</table>

Table 2: Recall rate, cancer detection rate and specificity computed from the data in Table 1 as well as their 95% confidence intervals.
### Table 3: Relationship between the PMMA thicknesses, equivalent breast tissue thicknesses and glandularity of equivalent breast tissue[12].

<table>
<thead>
<tr>
<th>PMMA [mm]</th>
<th>Equivalent breast tissue [mm]</th>
<th>Glandularity of equivalent breast tissue [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>21</td>
<td>97</td>
</tr>
<tr>
<td>30</td>
<td>32</td>
<td>67</td>
</tr>
<tr>
<td>40</td>
<td>45</td>
<td>41</td>
</tr>
<tr>
<td>50</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>60</td>
<td>75</td>
<td>9</td>
</tr>
<tr>
<td>70</td>
<td>90</td>
<td>4</td>
</tr>
</tbody>
</table>

### Table 4: Results from the Region of South Denmark for grid-based screening and screening with PRIME.

<table>
<thead>
<tr>
<th>Populations</th>
<th>number of women screened (NWS)</th>
<th>number of women recalled (NWR)</th>
<th>number of women with cancer (NWC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B (Grid-based screening)</td>
<td>50,071</td>
<td>1,295</td>
<td>276</td>
</tr>
<tr>
<td>A (Screening with PRIME)</td>
<td>22,117</td>
<td>539</td>
<td>121</td>
</tr>
</tbody>
</table>

### Table 5: Recall rate, cancer detection rate and specificity as well as their 95% confidence intervals computed from the data in Table 4.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Recall rate (NWR/NWC)</th>
<th>Cancer detection rate (NWC/NWS)</th>
<th>Specificity (1−(NWR−NWC)/NWS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B (Grid-based screening)</td>
<td>2.59% (2.45-2.73)</td>
<td>0.55% (0.49-0.62)</td>
<td>97.96% (97.84-98.09)</td>
</tr>
<tr>
<td>A (Screening with PRIME)</td>
<td>2.44% (2.23-2.64)</td>
<td>0.55% (0.45-0.64)</td>
<td>98.11% (97.93-98.29)</td>
</tr>
</tbody>
</table>

### Table 6: Differences of recall rate, cancer detection rate and specificity between the two study populations as well as the 95% confidence intervals of the differences computed from the data in Table 4 (pp denotes percentage points).

<table>
<thead>
<tr>
<th>Populations</th>
<th>Recall rate (NWR/NWS)</th>
<th>Cancer detection rate (NWC/NWS)</th>
<th>Specificity (1−(NWR−NWC)/NWS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference A−B</td>
<td>-0.15pp</td>
<td>0.00pp</td>
<td>0.15pp</td>
</tr>
<tr>
<td>95% CI of difference A−B</td>
<td>2.44% (2.23-2.64)</td>
<td>0.55% (0.45-0.64)</td>
<td>98.11% (97.93-98.29)</td>
</tr>
<tr>
<td>PMMA Breast</td>
<td>Tube</td>
<td>Target/filter</td>
<td>mAPRIME</td>
</tr>
<tr>
<td>-------------</td>
<td>------</td>
<td>---------------</td>
<td>---------</td>
</tr>
<tr>
<td>tissue (mm)</td>
<td>Voltage[kV]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>21</td>
<td>25</td>
<td>W/Rh</td>
</tr>
<tr>
<td>30</td>
<td>32</td>
<td>27</td>
<td>W/Rh</td>
</tr>
<tr>
<td>40</td>
<td>45</td>
<td>28</td>
<td>W/Rh</td>
</tr>
<tr>
<td>50</td>
<td>60</td>
<td>32</td>
<td>W/Rh</td>
</tr>
<tr>
<td>60</td>
<td>75</td>
<td>32</td>
<td>W/Rh</td>
</tr>
<tr>
<td>70</td>
<td>90</td>
<td>32</td>
<td>W/Rh</td>
</tr>
</tbody>
</table>

Table 7: The measured entrance surface air kerma (ESAK) for all breast tissue thicknesses and difference between the ESAK of PRIME (grid-less) and grid-based acquisitions.

<table>
<thead>
<tr>
<th>BTE (mm)</th>
<th>g-factor</th>
<th>s-factor</th>
<th>c-factor</th>
<th>ESAK(mGy)</th>
<th>AGD(mGy)</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PRIME</td>
<td>GRID</td>
<td>PRIME</td>
<td>GRID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>0.50</td>
<td>1.04</td>
<td>0.91</td>
<td>0.84</td>
<td>1.32</td>
<td>0.39 0.62 36.4</td>
</tr>
<tr>
<td>32</td>
<td>0.39</td>
<td>1.04</td>
<td>0.95</td>
<td>1.35</td>
<td>1.72</td>
<td>0.52 0.66 21.5</td>
</tr>
<tr>
<td>45</td>
<td>0.29</td>
<td>1.04</td>
<td>1.04</td>
<td>2.37</td>
<td>2.9</td>
<td>0.73 0.89 18.3</td>
</tr>
<tr>
<td>60</td>
<td>0.24</td>
<td>1.04</td>
<td>1.14</td>
<td>3.26</td>
<td>3.88</td>
<td>0.91 1.09 16.0</td>
</tr>
<tr>
<td>75</td>
<td>0.17</td>
<td>1.04</td>
<td>1.23</td>
<td>5.25</td>
<td>6.12</td>
<td>1.11 1.30 14.2</td>
</tr>
<tr>
<td>90</td>
<td>0.15</td>
<td>1.04</td>
<td>1.26</td>
<td>9.54</td>
<td>11.03</td>
<td>1.93 2.23 13.5</td>
</tr>
</tbody>
</table>

Table 8: The calculated AGD and difference between the PRIME (grid-less) and grid-based AGD for all breast tissue thicknesses, BTE= breast tissue equivalent.