Patient dose reduction combining tomosynthesis with synthetic instead of standard mammography

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Aims and objectives

Background

Clinical evidence about benefits of using digital breast tomosynthesis (DBT) in screening application has been mainly obtained comparing clinical performance of standard mammography alone (FFDM) with the combinations of DBT and FFDM [1,2,3]. This means that most of the screening DBT studies included the acquisition of both DBT and FFDM examinations in two views (cranio-caudal - CC, and medio-lateral oblique - MLO), with the consequent increase of radiation dose compared to a single examination.

As the systematic application in population-based screening programs of the (DBT + FFDM) protocol would have unavoidably doubled (at least) population dose, DBT manufacturers have developed reconstruction algorithms capable to generate a pseudo-2D image from the DBT dataset, similar to a standard mammogram acquired using x-rays; this allows to obtain a synthetic mammography (SM) examination to be used in combination with DBT, with no need for extra radiation dose [4,5].

Comparable cancer detection rate (CDR) for the combination of DBT and synthetic mammography, (DBT+SM), versus the combination of DBT and standard x-ray mammography, (DBT+FFDM), was found by Skaane and colleagues and by Bernardi and colleagues in two different screening trials [6,7].

Results from clinical datasets comparing per-view radiation dose by DBT and FFDM for two different clinical systems, have shown that, on the average, dose for one DBT view is between the same as the dose for one FFDM view [8], and 40% higher [9].

Study goal

The purpose of this study was to quantify the effect of using tomosynthesis (DBT) with synthetic mammography (SM) instead of DBT with standard x-ray mammography (FFDM) on the total patient-specific mean glandular dose (psMGD), considering different possible clinical protocols.
Methods and materials

Study population and breast imaging

1171 consecutive women were taken from the STORM-2 screening trial aiming to compare clinical performance of FFDM vs. the combination of DBT and FFDM. For each view (cranio-caudal, CC, and medio-lateral oblique, MLO) and breast (left and right), both FFDM and DBT images were acquired with the same breast position and under the same compression force. Single breast positioning for both FFDM and DBT guaranteed the same geometry and consequently the best condition to compare clinical information provided by the two modalities, as well as radiation dose. All FFDM and DBT examinations were acquired by a Selenia Dimensions system (Hologic, Bedford, MA, USA; AWS software version 1.7.4.5), using the automatic exposure control (AEC), i.e. the device in charge for the selection of technique factors (anode/filter combination, kV_p and mAs values) with the aim of ensuring an appropriate image quality while controlling radiation dose. The role of AEC in both FFDM and DBT is played by the image detector itself, which allows, on the basis of a short pre-exposure, to determine, the breast attenuation map and select suitable exposure parameters. Hologic DBT is obtained by 15 projections in 15° (±7.5°), with no antiscatter grid.

Patient-specific mean glandular dose (psMGD)

The parameter used for x-ray breast dosimetry is usually the mean (or average) glandular dose (MGD or AGD), i.e. the absorbed dose by the glandular tissues within the breast during x-ray based imaging.

MGD is estimated by multiplying the incident air kerma at the upper surface of the breast by a number of conversion factors obtained by Monte Carlo techniques, counting for breast characteristics (compressed thickness and composition) and x-ray beam properties (anode/filter combination, half value layer - HVL).

In Europe, the formalism to calculate mammography MGD was developed by Dance and colleagues [10,11], and given by the following formula:

\[
\text{MGD}_{\text{FFDM}} = K \times g \times c \times s
\]

where K is the incident air kerma at the upper surface of the breast, g is the conversion factor for a breast of 50% glandularity at the specified HVL, and the factors c and s correct for breast composition (glandularity) and choice of x-ray spectrum (target/filter...
combination), respectively [12]. In the Dance's model, the factor \( c \) is 1 for 50% breast glandularity, \( c > 1 \) for glandularity < 50% and \( c < 1 \) for glandularity >50%. In Fig. 1 on page 8 \( g \) and \( c \) factors are shown as a function of beam HVL, as reported in the paper published by Dance et al in 2000 [10]. For most of the spectra considered the \( s \)-factor was in the range 1.000-1.062 [12].

![Fig. 1](image)

**Fig. 1**: (Left) \( g \)-factor for varying breast thickness and HVL values. (Right) \( c \)-factors for a 5 cm compressed breast thickness for varying breast glandularity and HVL values. Data from Dance et al, 2000 [10].


The same formalism was maintained by Dance and colleagues with the introduction of DBT, including additional multiplying factor counting for the different angles of the DBT low-dose projections [13]:

\[
\text{MGD}_{\text{DBT}} = K_{\text{TOTAL}} \times g \times c \times s \times T
\]

where \( K_{\text{TOTAL}} \) is the total air kerma at the breast entrance obtained with the x-ray tube at the 0° position and using the total current \( x \) exposure time (mAs) as for the full DBT acquisition, and \( T \) is the angular factor obtained by correcting for the absorption changes related to the different angled projections during DBT acquisition. For a 5 cm compressed breast thickness the \( T \)-factor is between 0.995 and 0.968 for the minimum and maximum angular range (15° and 50°) available among commercial systems.
A pictorial summary of parameters contributing to the estimation of MGD is provided in Fig. 2 on page 8.

**Fig. 2**: Pictorial description of factors contributing to the mean glandular dose (MGD).

**References**: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

To be "patient-specific", MGD needs to take into account the absorption properties of individual breasts. While compressed breast thickness is measurable from the height of the compression paddle and is normally available by any mammography system (provided that appropriate calibration had been performed), breast density is not really measurable. In the past, most of dosimetric models assumed that the "typical breast" was composed 50% by glandular and 50% by adipose tissue (so-called 50-50 model). Afterwards, Yaffe et al demonstrated that the 50-50 breast model is not representative of an "average breast composition", as 95% of women have breast density below 45% [14]. More recently, quantitative software tools have been developed to determine volumetric breast density (VBD) from x-ray breast images (FFDM or DBT), with the major advantage of eliminating inter-observer variability which is unavoidably present when breast density is estimated by human observers using categorical scales [15]. Quantitative breast density can also be used to determine the c-factor more accurately and allow the estimation of patient-specific MGD.
Volpara software

Volpara is a software tool whose original purpose was to quantify volumetric breast density from mammography images. Its algorithm uses a model of the physics of digital mammography to work backwards from the pixel value in the image to the x-ray attenuation between the image detector and the x-ray source. From there, it calculates the types of tissue that must have been present between the detector and the x-ray source. This is a complex process that includes, for example, compensation for beam hardening and scattered radiation. From the compressed breast thickness reported in the image DICOM header and the attenuation components (glandular and flat tissue) measured at each image pixel, the volume of fibroglandular tissue and the breast volume are generated, and the VBD value (Fibroglandular Tissue Volume / Volume of Breast) is calculated [16]. More recently, Volpara was implemented to provide also patient-specific MGD. In order to do that, and in particular to determine the c-factor value, VBD needs to be converted in breast glandularity. Breast glandularity is an area-based parameter of breast density that is obtained by Volpara removing the contribution of the fatty breast edge and the subcutaneous fat from the volume of breast, and projecting the volume of glandular tissue onto a plane [17]. Volpara applies the same algorithm to compute psMGD by both FFDM and DBT; for DBT only the 0°-projection is used.

Method

The unprocessed images FFDM and DBT images of the 1171 patients included in the study were analyzed by Volpara v 1.5 (Volpara) to determine volumetric breast density, derive breast glandularity, and calculating patient specific mean glandular dose (psMGD) for each view.

The MGD values corresponding to the radiation dose absorbed for each view by a same patient were added together to obtain the psMGD of each modality, and psMGD distributions compared for FFDM and DBT.

Moreover, as most studies using tomosynthesis for screening published so far, have considered the combination of DBT with standard mammography, radiation dose corresponding to three different clinical protocols were evaluated, using DBT in two-views (CC+MLO) or in one-view (MLO) combined with mammography, or assuming to acquire only DBT in two-views and reconstruct synthetic mammography images from tomosynthesis:
1. Tomosynthesis in two-views used in combination with standard mammography in two-views (DBT\(_{(LCC+LMLO+RCC+RMLO)}\)+FFDM\(_{(LCC+LMLO+RCC+RMLO)}\))

2. Tomosynthesis in one-view used in combination with standard mammography in two-views (DBT\(_{(LMLO+RMLO)}\)+FFDM\(_{(LCC+LMLO+RCC+RMLO)}\))

3. Tomosynthesis in two-views used in combination with synthetic mammography in two-views (DBT\(_{(LCC+LMLO+RCC+RMLO)}\)+SM\(_{(LCC+LMLO+RCC+RMLO)}\))

**Statistical analysis**

\((HVL, mAs)\) pairs for each view were analyzed as a function of breast thickness for both FFDM and DBT.

Distributions of compressed breast thickness and volumetric breast density were described and the correlation between VBD and breast glandularity analyzed.

psMGD distributions were inspected for the individual modalities, as well for the three combinations previously listed. Significance of differences between psMGD distributions were tested by a Wilcoxon paired test. A p-value lower than 0.05 was considered statistically significant.

The ratio between psMGD related to each combination of modalities and the psMGD of FFDM as reference standard was calculated for each patient and the distribution of ratios analyzed to evaluate dose changes compared to FFDM; the same was done taking the combination of 2-view DBT and 2-view FFDM as reference standard.

Statistical analysis was performed by byMedCalc Statistical Software v. 17.11.5, and by OriginPro 2017.
Fig. 1: (Left) g-factor for varying breast thickness and HVL values. (Right) c-factors for a 5 cm compressed breast thickness for varying breast glandularity and HVL values. Data from Dance et al, 2000 [10].

Fig. 2: Pictorial description of factors contributing to the mean glandular dose (MGD).

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Fig. 3: (Top) Half value layer (HVL) as a function of breast thickness for FFDM and DBT; HVL is driven by anode/filter combination and tube voltage. (Bottom) Tube current x exposure time (mAs) as a function of breast thickness for FFDM and DBT.

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**Fig. 4:** (Left) Distribution of overall compressed breast thickness; (Right) Mean and standard deviation of compressed breast thickness for each single view, laterality, type of views (CC, MLO).

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Fig. 6: Patient-specific MGD distributions (histograms and box plots) for FFDM and DBT.

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Fig. 7: Distributions of patient-specific MGD assuming different clinical protocols for DBT: (red) combination of 2-view DBT with 2-view FFDM; (blue) combination of 1-view DBT with 2-view FFDM; (yellow) combination of 2-view DBT with 2-view synthetic mammography (SM).

Table 2: Summary table of dose increase associated to the three DBT clinical protocols compared to standard mammography and of dose reduction obtained replacing standard FFDM with synthetic mammography (SM).
Results

Automatic Exposure Control

Fig. 3 on page 20 illustrates the automatic exposure control (AEC) operation for FFDM and DBT respectively, showing how half value layer (HVL) and mAs are selected as a function of compressed breast thickness.

Fig. 3: (Top) Half value layer (HVL) as a function of breast thickness for FFDM and DBT; HVL is driven by anode/filter combination and tube voltage. (Bottom) Tube current x exposure time (mAs) as a function of breast thickness for FFDM and DBT.

References: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

It can be noticed that the AEC behaves differently with FFDM and with DBT: both HVL and mAs values increase as breast thickness increases, but HVL increment is steeper for DBT compared to FFDM, while the overall DBT mAs values are flatter than for FFDM, as breast thickness changes. This is obtained by using more penetrating x-ray beams with DBT (heavier filtration and higher kVp values) than those used with FFDM; this choice allows the achievement of a sufficient detector dose level per each DBT projection, while keeping the overall radiation dose reasonably low.
Breast thickness and density

Overall mean breast thickness was (48.0 ± 11.8) mm, with small differences among individual views and between left and right, and CC and MLO views (Fig. 4 on page 20).

![Graph showing distribution of breast thickness](image)

**Fig. 4**: (Left) Distribution of overall compressed breast thickness; (Right) Mean and standard deviation of compressed breast thickness for each single view, laterality, type of views (CC, MLO).

**References**: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

The g-factor in the MGD equations can be obtained from each (HVL, breast thickness) pair using tabulated values in papers published by Dance and colleagues [10-13]. The c-factor in MGD equations requires that breast glandularity is estimated; as previously remarked, breast glandularity is an "area-based" estimation of breast density, which is by definition a volumetric measurement. As represented in Fig. 5 on page 21, Volpara software automatically calculates glandularity from volumetric breast density by removing the contribution of both the fatty breast edge and the subcutaneous fat from the volume of breast and projecting the volume of glandular tissue onto a plane. Figure 6 shows distributions of both volumetric breast density and glandularity. Both the distributions are skewed, but the two parameters run on different scales: while VBD is systematically below 50%, breast glandularity ranges between 0 and 100%. Mean VBD was found to be 13.0%, median is 11.5%, and the 95th percentile 27.2%.
Glandularity and VBD are well correlated (Pearson’s $r = 0.97067$), with a linear relationship between the two parameters ($R^2 = 0.94219$), showing that glandularity is about twice VBD.

![Diagram of Volumetric Breast Density (3D) and Glandularity (2D)](image)

**Fig. 5**: Distributions of volumetric breast density (VBD) and breast glandularity, and correlation between the two parameters.

**References**: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

**Radiation dose**

Total radiation dose (LCC + LMLO + RCC + RMLO) was significantly higher ($p<0.0001$) for DBT than for FFDM: mean $psMGD_{DBT} = (7.54\pm2.46)$ mGy vs. mean $psMGD_{FFDM} = (5.52\pm1.78)$ mGy; median $psMGD_{DBT} = 7.00$ mGy, range $= [3.95 - 16.96]$ mGy vs. median $psMGD_{FFDM} = 5.15$ mGy, range $= [2.62 - 13.22]$ mGy. Distributions of patient-specific...
MGD (total per-patient dose) are shown in Fig. 6 on page 22, as histograms and box plots.

**Fig. 6**: Patient-specific MGD distributions (histograms and box plots) for FFDM and DBT.

**References**: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

Considering the combinations of DBT with either FFDM or SM, according to the clinical protocols previously described, (mean±standard deviation) psMGD, median psMGD, and psMGD ranges were those reported in Table 1 on page 24.

All differences were statistically significant.
Table 1: Summary table of different statistical descriptors (mean±standard deviation, median, and range) of psMGD distributions for the three DBT protocols.

References: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

Distributions of patient-specific MGD for the three DBT clinical protocols are provided in Fig. 7 on page 23.

Fig. 7: Distributions of patient-specific MGD assuming different clinical protocols for DBT: (red) combination of 2-view DBT with 2-view FFDM; (blue) combination of 1-view DBT with 2-view FFDM; (yellow) combination of 2-view DBT with 2-view synthetic mammography (SM).

References: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

Patient-specific MGD for 2-view DBT + 2-view FFDM was between 2 and 3 times the dose for FFDM, while dose for 1-view DBT + 2-view FFDM was between 1.4 and 2 times dose for FFDM. The 2-view DBT+ 2-view SM protocol delivered dose 0.9-2 times the dose for FFDM (Table 2 on page 24).
Table 2: Summary table of dose increase associated to the three DBT clinical protocols compared to standard mammography and of dose reduction obtained replacing standard FFDM with synthetic mammography (SM).

References: Breast Radiology Unit, Veneto Institute of Oncology (IRCCS) - Padua/IT

However, considering the combination of DBT in 2-views with standard FFDM as reference standard, the use of synthetic mammography in place of standard mammography leads to an average dose reduction by 42%. This confirms the relevant effect of synthetic mammography in reducing dose compared to the (2-view DBT + 2-view FFDM) protocol.

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Reference Standard</th>
<th>Mean</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-view DBT+2-view FFDM</td>
<td>FFDM</td>
<td>2.38</td>
<td>2.37</td>
<td>1.89</td>
<td>2.95</td>
</tr>
<tr>
<td>1-view DBT+2-view FFDM</td>
<td>FFDM</td>
<td>1.69</td>
<td>1.68</td>
<td>1.43</td>
<td>2.03</td>
</tr>
<tr>
<td>2-view DBT+2-view SM</td>
<td>FFDM</td>
<td>1.38</td>
<td>1.37</td>
<td>0.89</td>
<td>1.95</td>
</tr>
<tr>
<td>2-view DBT+2-view SM</td>
<td>2-view DBT+2-view FFDM</td>
<td>0.42</td>
<td>0.42</td>
<td>0.34</td>
<td>0.53</td>
</tr>
</tbody>
</table>
Fig. 3: (Top) Half value layer (HVL) as a function of breast thickness for FFDM and DBT; HVL is driven by anode/filter combination and tube voltage. (Bottom) Tube current x exposure time (mAs) as a function of breast thickness for FFDM and DBT.

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Fig. 4: (Left) Distribution of overall compressed breast thickness; (Right) Mean and standard deviation of compressed breast thickness for each single view, laterality, type of views (CC, MLO).

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**Fig. 5**: Distributions of volumetric breast density (VBD) and breast glandularity, and correlation between the two parameters.

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Table 2: Summary table of dose increase associated to the three DBT clinical protocols compared to standard mammography and of dose reduction obtained replacing standard FFDM with synthetic mammography (SM).
<table>
<thead>
<tr>
<th>DBT Protocol</th>
<th>(Mean±SD) psMGD (mGy)</th>
<th>Median psMGD mGy</th>
<th>psMGD range (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBT(LCC+LMLO+RCC+RMLO)+FFDM(LCC+LMLO+RCC+RMLO)</td>
<td>13.06±4.15</td>
<td>12.02</td>
<td>(6.58, 28.5)</td>
</tr>
<tr>
<td>DBT(LMLO+RMLO)+FFDM(LCC+LMLO+RCC+RMLO)</td>
<td>9.31±3.03</td>
<td>8.52</td>
<td>(4.60, 20.59)</td>
</tr>
<tr>
<td>DBT(LCC+LMLO+RCC+RMLO)+SM(LCC+LMLO+RCC+RMLO)</td>
<td>7.54±2.46</td>
<td>7.00</td>
<td>(3.96, 16.98)</td>
</tr>
</tbody>
</table>

**Table 1:** Summary table of different statistical descriptors (mean±standard deviation, median, and range) of psMGD distributions for the three DBT protocols.

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Conclusion

Patient-specific MGD is significantly reduced when DBT is combined with synthetic mammography in place of standard mammography.
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References

