Mammographic density estimation: one-to-one comparison between digital mammography and digital breast tomosynthesis using a fully automated software and magnetic resonance imaging calibration

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Purpose

The purpose of our study was to compare breast density on full-field digital mammography (FFDM), digital breast tomosynthesis (DBT), and Magnetic Resonance Imaging (MRI) in the same patients using semi-automated software.
Methods and Materials

The study was approved by the local ethics committee (National Institute for Cancer Research) and written informed consent was obtained from all participating women.

Patients

This was a prospective study of women attending for diagnostic imaging (March 2010 to October 2012). FFDM, DBT, and MRI images were obtained in the participating women on the same day to reduce variations related to hormonal status. After FFDM, DBT, and MRI further workup was done when indicated.

Digital mammography

For FFDM (Hologic DimensionsTM System, Bedford, Massachusetts, USA), the breast was positioned for mediolateral oblique and craniocaudal views and was compressed by using the standard mammographic compression force. After acquisition, digital mammograms were available in an unprocessed, raw format, with pixel values linearly proportional to the X-ray exposure at the detector, as well as in a processed format obtained by using an embedded adaptive histogram equalisation method.

Digital breast tomosynthesis

DBT was performed by three dedicated technologists using a commercially available device (Hologic SeleniaTM DimensionsTM System, Bedford, MA, USA). The device used consists of a custom-designed high-power (mA) tungsten (W) anode X-ray tube, and X-ray filters of rhodium (Rh), silver (Ag) and aluminium (Al). These different filters are used in 2D and 3D imaging, and produce optimal X-ray spectra based on breast thickness/composition and imaging modes. With this achievement, patient radiation exposure is minimised, maintaining high image quality and low exposure. The X-ray tube moves over a 15° arc while the breast is compressed, taking a series of ultra-low-dose mammograms. The projections are then combined to create a full 3D image set of the breast, with 1-mm slices through the breast. Each DBT data set consisted of 15 projection images.

MRI

MRI was performed for equivocal or suspicious findings on X-ray mammography or breast ultrasound (US) following European recommendations. The women were examined between days 5 and 15 of their menstrual cycle. Women with incomplete examination or non-interpretable images, i.e. due to artefacts, were not included in the study. All MRI examinations were performed on a GE 3.0-T HDx Signa scanner using a dedicated eight-channel bilateral breast coil (General Electric Medical Systems, Milwaukee, WI, USA) with the patient in prone position without compression. Each MRI examination included...
a T1-weighted sequence for anatomical reference. The T1-weighted sequence was acquired with a 3D fast spoiled-gradient-recalled echo sequence with parallel imaging [Volume Imaging for Breast Assessment (VIBRANT)], repetition time (TR) = 6.2 ms, echo time (TE) = 3 ms; flip angle =10°; 350×350 matrix, and 90-s scan time. To assess breast density, IDEAL(iterative decomposition of water and fat with echo asymmetry and least squares estimation) sequences were used. These sequences are considered suitable to separate the fatty nonglandular tissue from the water content of the true glandular tissue . Imaging parameters for IDEAL sequences were: repetition time (TR) = 4380 ms, echo time (TE) = 130.872 ms; flip angle =90°; 360×360 matrix, and 600-s approximately of scan time.

BI-RADS density classification

Breast density evaluation was performed by two radiologists independently (M.C. and A.T.) with 21 and 6 years of experience in breast examination and with more than 6000 FFDM examinations reported every year. Inter-observer agreement between the two radiologists was calculated. The evaluation was made using the conventional quantitative BI-RADS classification, which has four density categories according to the parenchymal structure (D1:0-25 %; D2: 26-50 %; D3: 51-75 %; D4:76 %).

Breast density analysis with semi-automated software

The data set comprised the digital mammograms and the DBT projections and the MRI images obtained in 48 patients. Only images of the unaffected side were included in the analysis. None of the women had bilateral pathological findings. All DBT projections and MRI images were analysed and the mean value obtained was used for comparison with FFDM. For analysis we used software previously employed on full digital and analogical mammograms. We performed the evaluation using the maximum entropy thresholding method developed by Shannon because we considered this method to be the most suitable to compare FFDM and DBT. We performed the evaluation with the semi-automatic software because we noted that the fully automated software excluded some MRI images from the analysis due to artefacts. The digital images obtained were analyzed by two radiologists blindly from each other after an appropriate training with this method. After the first evaluation, measurements were repeated after 2 months to assess intraobserver variability; this method has been previously described.

Statistical analysis

We assessed the relationship between the MRI and DBT percent density (volumetric) and projection-based FFDM percent density measurements, using correlation and regression analysis to calculate the correlation factor (r) and the coefficient of determination (R2). P values <0.05 were considered statistically significant. Systematic and absolute differences between density estimates from FFDM, DBT, and MRI were plotted against the average density estimate using Bland-Altman statistics. The intra- and inter-observer agreement was then calculated; kappa (#) statistics were used and # values were
reported as weighted # with linear weights. 95 %confidence intervals (95 %CI) and standard errors were also calculated. The standard errors reported are the appropriate standard errors for testing the hypothesis that the underlying value of the weighted kappa is equal to a pre-specified value other than zero. Agreement was defined on the basis of Fleiss classification as follows: <0.40, poor; 0.40-0.59, moderate; 0.60-0.75, good; >0.75, excellent. Statistical analysis has been performed with statistical software (MedCalc Version 12.3.0—1993-2012 MedCalc Software bvba-Last modified: June 27, 2012-MedCalc Software, Broekstraat 52, 9030 Mariakerke, Belgium).
Results

The percent MRI and DBT mammographic density findings showed a positive linear correlation (correlation factor $r=0.95$, $P<0.0001$), based on images of 48 breasts from 48 women (mean age, 41 years; range, 35-67 years).

The percent FFDM and DBT mammographic density findings showed a positive linear correlation (correlation factor $r=0.97$, $P<0.0001$).

The percent MRI and FFDM mammographic density findings also showed a positive linear correlation (correlation factor $r=0.87$, $P<0.0001$).

Linear regression analysis, allowing for the non-independence of DBT and MRI images from each woman, gave the following regression equation:

$$MRI \text{ percent density} = 0.3198 + 0.9848 \times DBT \text{ percent density}$$

MRI-measure of the percentage density was slightly higher than that estimated by DBT.

The 95% CI for the slope was 0.88-0.99, $p<0.001$. The coefficient of determination $R^2$ was high=0.89.

Multiple regression analysis using BIRADS evaluation on a four grade scale as a dependent variable confirmed that there was a strong positive linear relationship among MRI-density, FFDM and DBT density. The overall coefficient of determination was $R^2=0.93$; correlation coefficients ($r$) were: 0.95 for FFDM, 0.94 for DBT and 0.83 for MRI. All these values were statistically significant ($p<0.05$) in the model using BIRADS as dependent variable.

**FFDM versus DBT versus MRI**

FFDM overestimated breast density in 15.1% in comparison to DBT and in 16.2% in comparison to MRI. The 95% limits of agreement among the three methods were 3.22 and 28.90.

The mean values and standard deviation of percentage breast density were 66.1±22.2 for FFDM, 54.3±21.5 for DBT, and 53.4±21.5. The differences in breast percentage density between FFDM and DBT, and also between DBT and MRI, were highly significant ($P<0.0001$). On the contrary differences in breast percentage density between DBT and MRI were not statistically significant ($P>0.05$).

Overall agreement among FFDM, DBT, MRI and radiologists’ BI-RADS was good ($k=0.80$ for each of two radiologists). Using the BI-RADS method, intra-observer and inter-observer agreement of the two radiologists in the evaluation of breast density were
considered to be very good (intra-observer: reader 1, $k=0.81$; reader 2, $k=0.86$; inter-observer: reader 1 versus reader 2, $k=0.91$).
**Fig. 1:** Comparison of breast density values (percent) estimated with maximum entropy thresholding method for three breast imaging modalities (FFDM full-field digital mammography, DBT digital breast Tomosynthesis, MRI magnetic resonance imaging).

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Fig. 2

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Conclusion

Our study reports a comparison of breast density estimated on FFDM, DBT, and MRI in the same patient cohort.

Breast density values may be underestimated on DBT and MRI images in comparison to FFDM, however, all three methods were well-correlated in measurement of tissue density. Of importance, we did not observe significant differences between MRI and DBT percent densities, suggesting that these modalities may provide equally robust means to measure percentage breast density.

These data, which suggest that various imaging modalities currently available in clinical practice can determine breast density, have the potential to influence clinical and research studies that include breast density assessment in various clinical and epidemiologic applications.
References


