## Abridged Clinical Results

### Quantra Breast Density Software

This document includes summaries of many documented clinical studies involving Quantra™ software. The summaries are meant to be informative, but are not necessarily complete. When possible, please refer to the original studies for more comprehensive details.

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<td>Schmachtenberg C, Hammann-Kloss S, Bick U, Engelken F</td>
<td>Acad Radiol. 2015 Apr;22(4):447-52. doi: 10.1016/j.acra.2014.12.003. Epub 2015 Jan 10</td>
<td>&quot;Quantra and Volpara use different models for analysis of volumetric breast composition and produce different nominal results of FTV and PD, both methods are highly correlated and show very good to excellent agreement in quartile assignment of all parameters measured. Both methods show a similar association with patient age and similar reproducibility. Both methods can be mapped onto each other using the equations suggested.&quot;</td>
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<td>Sanderson M, O'Hara H, Foderingham N, Dupont WD, Shu XO, Peterson N, Fair AM, Disher AC</td>
<td>Cancer Causes Control. 2015 Feb;26(2):303-9. doi: 10.1007/s10552-014-0502-3. Epub 2014 Nov 25</td>
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<td>&quot;The study showed excellent reproducibility of breast density measurement with the Volpara and Quantra algorithms and moderate reproducibility with the Cumulus ABD and CumulusV algorithms. The excellent reproducibility of automated breast density measurements indicates that they would be well suited for inclusion in a breast cancer risk model.&quot;</td>
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<td>Mammographic Breast Density: Comparison of Methods for Quantitative Evaluation</td>
<td>Morrish OW, Tacher L, Black R, Willeber P, Duffy SW, Gilbert FJ</td>
<td>Radiology. 2015 Jan 5;141508</td>
<td>&quot;Automated techniques for measuring breast density show good correlation, but these are poorly correlated with observer's scores. However automated techniques do give different results that should be considered when informing patient personalized imaging.&quot;</td>
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<td>Radiological assessment of breast density by visual classification (BI-RADS) compared to automated volumetric digital software (Quantra): implications for clinical practice</td>
<td>Regini E, Mariscotti G, Durando M, Cioni G, Luparia A, Campanino PP, Bianchi CC, Bergamasco L, Fonio P, Gandini G</td>
<td>Radiol Med. 2014 Oct;119(10):741-9. doi: 10.1007/s11547-014-0390-3. Epub 2014 Mar 8</td>
<td>&quot;Quantra seems to provide a more accurate assessment of breast density in clinical practice, and may allow better correlation between density and breast disease. However, to provide a practical criterion for correlating the BI–RADS classification and the Quantra results, an appropriate cut-off value (set at 21%) is required that separates dense from non-dense breasts.&quot;</td>
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<td>Digital mammographic density and breast cancer risk: a case-control study of six alternative density assessment methods</td>
<td>Eng A, Gallant Z, Shepherd J, McCormack V, Li J, Dowsett M, Viniciusmo S, Allen S, dos-Santo-Silva I</td>
<td>Breast Cancer Res. 2014 Sep 20;16(5):439. doi: 10.1186/s13058-014-0439-1</td>
<td>&quot;Fully-automated methods are valid alternatives to the labour-intensive 'gold standard' Cumulus for quantifying density in FFDM. The choice of a particular method will depend on the aims (for example, aetiological investigations versus risk prediction) and setting (for example, research versus clinical), but the same approach will be required in longitudinal assessments of density.&quot;</td>
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<td>&quot;Fibroglandular tissue volume (FTV) and percent density (PD) change significantly during the perimenopausal period but remain relatively constant before and thereafter. Median total breast volume consistently increases with age and further contributes to changes in breast density. HRT use is associated with a significantly higher PD.&quot;</td>
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<td>Wang J, Azziza A, Fox B, Mallove S, Kifia C, Newitt D, Yitta S, Hydlon N, Kerlikowske K, Shepherd JA</td>
<td>PLoS One. 2013 Dec 4;8(12):e81653. doi: 10.1371/journal.pone.0081653. eCollection 2013</td>
<td>&quot;Volumetric breast density measures of total breast volume, fibroglandular volume, and percent fibroglandular volume from screening digital mammograms calculated from the techniques used in this study are in moderate to substantial agreement with the volume measures derived from MRI. The SXA measure of density showed a higher association to MRI than Volpara or Quantra density measures. However, classification of women by volumetric density by any of the three mammographic techniques is comparable to classifications by MRI density.&quot;</td>
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<td>Rofo. 2012 Oct;184(10):911-8. Epub 2012 Jun 18. The mean calculated AGD per exposure in 3D imaging mode was on average 34% higher than the 2D imaging mode for patients examined with the same compressed breast thickness. The mean calculated AGDs for both 2D and 3D imaging modes were lower than the dose limits recommended by ACR, European protocols and the diagnostic reference level for Germany.</td>
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<td>IWDM 2012, LNCS 7361, pp127-133, 2012 © Springer-Verlag Berlin Heidelberg 2012. This study was based on the premise that screening mammography could be made more effective by adapting the imaging modality and the interval to a woman's individual risk of breast cancer. Breast density plays an important role, not only because it is an important risk factor, but also because it can be altered by lifestyle or other interventions.</td>
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<td>Publication</td>
<td>A First Evaluation for Breast Radiological Density Assessment by QUANTRA Software as Compared to Visual Classification: Ciatto D., Bernardi D., Calabrese M., et al.</td>
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<td>Breast (2012) doi:10.1016/j.breast.2012.01.005. Computer assessed breast density is absolutely reproducible, and thus to be preferred to visual classification.</td>
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<td>American Society for Reproductive Medicine 67th Annual Meeting, Orlando, FL, USA, October 2011. R2 Quantra and Subjective BIRAD readings are associated with each other. This relationship held regardless of race. R2 Quantra density did not differ between premenopausal and menopausal subjects, in contrast to other published data. This pattern also was persistent among racial groups.</td>
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<td>Oral Presentation</td>
<td>Correlation of Ethnicity with Breast Density as Assessed by Quantra**: D. Tzian, S. George, L. Wilkinson, R. Mehta, C. Lobo, A. Hainsworth, A. Sharma</td>
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<td>Royal College of Radiologists Breast Group Annual Scientific Meeting 2011. There is a statistically significant difference between the objectively measured breast densities between these three ethnic groups. This is of relevance to the assessment of breast cancer risk.</td>
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<td>Publication</td>
<td>A comparative study of volumetric breast density estimation in digital mammography and magnetic resonance imaging: Results from a high-risk population: Kontos D., Xing Y., Bakic P., Conant E., Maidment A</td>
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<td>Proceedings of SPIE Medical Imaging 2010, San Diego, CA, USA. DM [with Quantra] could provide reliable quantitative and automated volumetric breast density measures that could potentially be used as an imaging biomarker for breast cancer risk estimation during breast cancer screening for the general population.</td>
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<td>The 10th International Workshop of Digital Mammography, IWDM 2010, Girona Catalonia, Spain, June 2010. The current algorithm has an agreement rate of 62% matching the BI-RADS score from doctors. This performance is similar to how radiologists agree among themselves with BI-RADS score.</td>
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<td>Scientific Poster</td>
<td>Quantitative Assessment of Breast Density: Comparing of Different Approaches: Qin N</td>
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<td>RSNA 2010, Chicago, IL, USA. High correlation between breast density estimates on R2 Quantra and MRI FCM suggested the former could be used as an effective and accurate application.</td>
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<td>European Congress of Radiology 2010, Vienna, Austria. &quot;Automated volumetric analysis confirms the link between urban and higher breast density, identified by subjective radiologist classification.&quot;</td>
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<td>Publication</td>
<td>A Comparative Study of Volumetric and Area-Based Breast Density Estimation in Digital Mammography: Results from a Screening Population: Deapina Kontos, Predrag R. Bakic, Raymond J. Acciaiatti, Emily F. Conant, and Andrew D.A. Maidment</td>
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<td>Digital Mammography © Springer-Verlag Berlin Heidelberg 2010. J. Marti' et al. (Eds.): IWDM 2010, LNCS 6136, pp 378-385, 2010. The strong correlation observed between the right and left breasts indicates that volumetric breast density measures computed with Quantra™ can provide consistent and fully-automated measures of breast density for women undergoing mammographic screening.</td>
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<td>Royal College of Radiology Breast Group 2009, Belfast, UK. Until now all methods available have been subjective or required manual delineation of tissue outlines. Quantra overcomes these issues and has proved to be such an effective, accurate and efficient application.</td>
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| Scientific Poster | Correlation of Age and HRT with Breast Density as Assessed by Quantra”  
Skippage PL, Wilkinson LS, Allen SD, Roche N, Dowsett M, A'Hern R  
Royal College of Radiology Breast Group 2009, Belfast, UK  
“Quantra has shown to be accurate and reproducible by its expected correlation with lifestyle and demographic data. Given its ease of acquisition and display this could be the future of breast density quantification in the digital age.” | 12   |
| Scientific Poster | Correlation of Age and HRT with Breast Density as Assessed by Quantra”  
Skippage PL, Wilkinson LS, Allen SD, Dowsett M, Roche N, A'Hern R  
RSNA 2009, Chicago, IL, USA  
“Quantra could be used to identify women with high density breasts who would benefit from early screening.” | 12   |
Rafferty E, Smith A, Niklason L  
RSNA 2009, Chicago, IL, USA  
“Volumetric breast density [Quantra] may provide an alternative method of determining breast density.” | 12   |
| Scientific Presentation | Validation of a New Automated Volumetric Breast Density Measurement System as a Marker of Breast Cancer Risk  
Pinker K, Perry N, Milner S, Mokbel K, Duffy S  
RSNA 2009, Chicago, IL, USA  
“Quantra automated volumetric breast density measurement is strongly associated with breast cancer risk in women aged under 50, but not in women aged 50 years or over.” | 13   |
| Scientific Poster | Qualitative and Quantitative Analysis of Fibroglandular Tissue in the Digital Environment  
10th National Congress of Breast Diseases, Izmir, Turkey 2009  
“We believe the relationship between the breast cancer and the fibroglandular tissue density can be evaluated more accurately if the volumetric breast program which provides 3D numerical measurement is used in this assessment.” | 13   |
| Publication | Volumetric Assessment of Breast Tissue Composition from FFDM Images  
“We have shown that the Quantra automated breast tissue measurement algorithm is internally consistent and that it has a high degree of agreement with external validation tests.” | 13   |

**Intraindividual comparison of two methods of volumetric breast composition assessment**  
Schmachtenberg C, Hammann-Kloss S, Bick U, Engelken F  

**SUMMARY OF PUBLICATION:**  
This study was done to compare the results of two software-based methods, Quantra and Volpara, for volumetric breast composition assessment. A retrospective analysis was done on 445 bilateral two-view (craniocaudal and mediolateral oblique) mammograms from a database of patients who were subjects in a longitudinal study on changes in breast composition with aging (20). The mammograms were acquired on the same mammography unit (GE Senographe 2000D, General Electric Company, Fairfield, CT) in the institution between August 2000 and December, 2009. Raw image data of all four views was analyzed with Quantra 2.0 and Volpara Research, version 1.4.3. The software determined breast volume (BV), fibroglandular tissue volume (FTV), and breast percent density (PD).  

The median and quartile ranges of both methods agreed well for BV but were different for FTV and PD, with Quantra showing much higher values of FTV and PD. The correlation of results obtained by both methods for BV, FTV, and PD was 0.99, 0.91, and 0.94, respectively. Intraclass correlation in the assignment of quartiles of BV, FTV, and PD was 0.96, 0.86, and 0.90, respectively. Both methods showed a similar association of FTV and PD with patient age and similar left-to-right correlation. Mapping of results onto each other using linear equations removed the systematic differences.  

The study concludes: “Quantra and Volpara use different models for analysis of volumetric breast composition and produce different nominal results of FTV and PD, both methods are highly correlated and show very good to excellent agreement in quartile assignment of all parameters measured. Both methods show a similar association with patient age and similar reproducibility. Both methods can be mapped onto each other using the equations suggested.”
Type 2 diabetes and mammographic breast density among underserved women
Sanderson M, O’Hara H, Foderingham N, Dupont WD, Shu XO, Peterson N, Fair AM, Disher AC


SUMMARY OF PUBLICATION:
This study was done to investigate the relationship between diabetes and mammographic breast density. A total of 175 premenopausal women and 288 postmenopausal women for included for analysis in this study. These women completed in-person interviews, body measurements, and full-field digital mammograms on a Hologic mammography unit from December 2011 to February 2014. Quantra, an automated algorithm for volumetric assessment of breast tissue was used to measure average percent breast density for the left and right breasts combined.

After adjustment for confounding variables, the mean percent breast density among premenopausal women with type 2 diabetes was non-significantly lower than that of women without type 2 diabetes however, there was no such association among postmenopausal women. The effect of type 2 diabetes in severely obese women (BMI > 35) appeared to differ by menopausal status with a reduction in mean percent breast density in premenopausal women, but an increase in mean percent breast density in postmenopausal women which could have been due to chance.

The study concludes: “Confirmation of our findings in larger studies may assist in clarifying the role of the insulin signaling breast cancer pathway in women with high breast density and ultimately target those women who will benefit most from primary and secondary prevention.”

Reliability of Automated Breast Density Measurements
Alonzo-Proulx O, Mawdsley GE, Patrie JT, Yaffe MJ, Harvey JA

Published: Radiology. 2015 Feb 25:141686

SUMMARY OF PUBLICATION:
This study was done to estimate the reliability of a reference standard two-dimensional area-based method and three automated volumetric breast density measurements using repeated measures. A prospective analysis of 32 women undergoing screening mammogram who also consented to a repeat craniocaudal exam was done. Breast density was measured by using an area based method (Cumulus ABD) and three automated volumetric methods (CumulusV [University of Toronto], Volpara [version 1.4.5; Volpara Solutions, Wellington, New Zealand], and Quantra [version 2.0; Hologic, Danbury, Conn]).

Discrepancy between the first and second breast density measurements (D1–2) was obtained for each algorithm by subtracting the second measurement from the first. The D1–2 values of each algorithm were then analyzed with a random-effects model to derive Bland-Altman–type limits of measurement agreement. Standard deviations for density measurement within the same breast were 3.32% (95% confidence interval [CI]: 2.65, 4.44), 3.59% (95% CI: 2.86, 4.48), 0.99% (95% CI: 0.79, 1.33), and 1.64% (95% CI: 1.31, 1.39) for Cumulus ABD, CumulusV, Volpara, and Quantra, respectively.

The study concludes: “The study showed excellent reproducibility of breast density measurement with the Volpara and Quantra algorithms and moderate reproducibility with the Cumulus ABD and CumulusV algorithms. The excellent reproducibility of automated breast density measurements indicates that they would be well suited for inclusion in a breast cancer risk model.”
Mammographic Breast Density: Comparison of Methods for Quantitative Evaluation
Morrish OW, Tucker L, Black R, Willsber P, Duffy SW, Gilbert FJ

Published: Radiology. 2015 Jan 5:141508

SUMMARY OF PUBLICATION:
This study was done to evaluate the results from two software tools for measurement of mammographic breast density and compare them with observer-based scores in a large cohort of women. Standard 2D digital mammograms (n = 36,281) from 8,867 women were obtained from the Tomosynthesis with digital Mammography, or TOMMY, trial in the United Kingdom National Health Service Breast Screening Program by using the full-field digital mammography system (Selenia™ Dimensions®, Hologic) that were installed in six centers in the United Kingdom. Breast density was assessed by 26 readers on a visual analog scale, giving a score ranging from 0% to 100%. Two software packages were used to assess the breast density on each mammogram (Quantra version 2.0, Hologic; and Volpara version 1.4.2, ŌtaKina Technology). The two automated methods were assessed for mutual agreement on measurements of total breast volume and fibroglandular tissue volume. Correlation between observer's measurements and the automated measurements was evaluated using Pearson Correlation Coefficient.

There is good agreement for overall breast volume when we compare two software tools, with Quantra giving a median value of 953.5 cm³ and Volpara giving a median value of 921.4 cm³ but there is less agreement for median fibroglandular tissue volume (Quantra, 93.0 cm³; and Volpara, 71.6 cm³). Pearson's Correlation Coefficient for between observer's scores and volumetric breast density estimated by Quantra and Volpara was 0.60 and 0.63.

The study concludes: "Automated techniques for measuring breast density show good correlation, but these are poorly correlated with observer's scores. However automated techniques do give different results that should be considered when informing patient personalized imaging."

Radiological assessment of breast density by visual classification (BI-RADS) compared to automated volumetric digital software (Quantra): implications for clinical practice


SUMMARY OF PUBLICATION:
This study was done to assess breast density on digital mammography and digital breast tomosynthesis according to the visual Breast Imaging Reporting and Data System (BI-RADS) classification, to compare visual assessment with Hologic's Quantra software for automated density measurement, and to establish the role of the software in clinical practice. In addition, the authors attempted to correlate breast density with Age, HRT usage and risk of occurrence of breast cancer.

A total of 200 mammograms performed in 2D and 3D modality were analyzed (100 with cancers and 100 without cancers). The patients underwent 2D and 3D imaging in a single compression using Hologic's Selenia™ Dimensions™ digital mammography system. A radiologist reviewed the images acquired in 2D and 3D modes in a single session and defined a visual density according to BI-RADS classification. The 2D images were subsequently processed by Quantra automatic software (Quantra™ 1.3, Hologic Inc, Bedford MA, USA). Breast density estimated by Quantra was correlated with age, use of hormone therapy, and increased risk of disease. The results showed that the breast density was negatively correlated to age (r = -0.44) and positively to use of hormone therapy (p = 0.0004). Quantra density was higher in breasts with cancer than in healthy breasts.

The study concludes: "Quantra seems to provide a more accurate assessment of breast density in clinical practice, and may allow better correlation between density and breast disease. However, to provide a practical criterion for correlating the BI–RADS classification and the Quantra results, an appropriate cut-off value (set at 21%) is required that separates dense from non-dense breasts."
Digital mammographic density and breast cancer risk: a case-control study of six alternative density assessment methods


SUMMARY OF PUBLICATION:
This study was done to compare various area and volume based methods of mammographic density measurement and association of these measurements with breast cancer risk. Three area-based approaches (BI-RADS, the semi-automated Cumulus, and the fully-automated ImageJ-based approach) and three fully-automated volumetric methods (Volpara, Quantra and single energy x-ray absorptiometry (SXA)) were used to analyze 3168 FFDM images from 414 cases and 685 controls. Cases were women with newly diagnosed breast cancer between April 2010 and July 2012. Controls were women who attended routine screening during the same period and were found to be breast cancer free. Breast cancer risk factors data were collected through questioners at the time of imaging. Association between breast cancer risk factors and density parameters was performed using linear regression models after adjustment of age and BMI.

All six density assessment methods showed that percent density (PD) was inversely associated with age, BMI, being parous and postmenopausal at mammography. PD was positively associated with breast cancer for all methods. For use of Quantra in breast density in regression model, the women in BIRADS IV category had on an average 3.94 times the risk of developing cancer compared to women with BIRADS I category. This factor was 8.26, 3.38, 2.99, and 2.55 for Volpara, Cumulus, SXA, Image J based methods. Increase in risk per standard deviation increment in density was estimated to be 1.40 for Quantra. The same value was 1.83, 1.58, 1.37 and 1.45 for Volpara, Cumulus, SXA and Image J based method.

The study concludes: “Fully-automated methods are valid alternatives to the labour-intensive ‘gold standard’ Cumulus for quantifying density in FFDM. The choice of a particular method will depend on the aims (for example, aetiological investigations versus risk prediction) and setting (for example, research versus clinical), but the same approach will be required in longitudinal assessments of density.”

Volumetric quantification of the effect of aging and hormone replacement therapy on breast composition from digital mammograms
Hammann-Kloss JS, Bick U, Fallenberg E, Engelken F


SUMMARY OF PUBLICATION:
The study was done to evaluate changes in breast composition that are attributed to aging and use of HRT using volumetric breast composition assessment estimated by Hologic’s Quantra software in a cohort of healthy women. A total of 764 consecutive mammograms of 208 non-HRT using women and 508 mammograms of 134 HRT-using women were analyzed using volumetric breast composition assessment software (Quantra™, Hologic Inc.). Fibroglandular tissue volume (FTV), breast volume (BV), and percent density (PD) were measured. Women were divided three age groups: a premenopausal (<46 years), a perimenopausal (46–55 years), and a postmenopausal (>55 years) for statistical analysis.

Total breast volume (BV) demonstrated positive rate of change for all age groups. Fibroglandular tissue volume (FTV) showed a fast decline in the age groups between 49 and 60 years. Patients who took HRT throughout the study had a significantly higher FTV and PD than controls. While there was a difference in the median rate of change of FTV between HRT-takers and controls, this was not statistically significant.

The study concludes: “Fibroglandular tissue volume (FTV) and percent density (PD) change significantly during the perimenopausal period but remain relatively constant before and thereafter. Median total breast volume consistently increases with age and further contributes to changes in breast density. HRT use is associated with a significantly higher PD.”
Agreement of mammographic measures of volumetric breast density to MRI


SUMMARY OF PUBLICATION:

This study was done to compare the agreement of three mammography based techniques of automated volumetric breast density measurement to MRI based volumetric breast density measurement. A total of 99 women undergoing screening mammography and screening MRI at the UCSF Medical Center within one year of each other were included in this study. Images from only left breast were used for this study. Four methods were used to assess volumetric breast density: a fuzzy-clustering segmentation method on MRI, the Single energy X-ray Absorptiometry (SXA) method, the Quantra method (Hologic, Inc., Bedford, MA, USA), and the Volpara method (Matakina, Wellington, New Zealand) on Full-Field Digital Mammography (FFDM) images. T1-weighted non-contrast fat-saturated images were acquired on either a 1.5 or 3 Tesla GE system (General Electric Medical Systems, Milwaukee, WI) using a bilateral phased-array breast coil (Medical Devices, Madison, WI) with women lying in a prone position. All mammograms were acquired on Hologic Selenia® FFDM system at UCSF.

All mammographic measurement of total breast volume (TBV) were highly correlated with the corresponding measure on MRI method. Quantra resulted in R² of 0.91 (PCC 0.95) for TBV using linear regression evaluation. The percentage value of volumetric density (%FTV) using Quantra correlated with R² of 0.51 (PCC 0.71). The comparison of quantile grouping based distribution of %FTV between Quantra and MRI showed in a substantial agreement between the two measurements with a kappa value of 0.62.

The study concludes: “Volumetric breast density measures of total breast volume, fibroglandular volume, and percent fibroglandular volume from screening digital mammograms calculated from the techniques used in this study are in moderate to substantial agreement with the volume measures derived from MRI. The SXA measure of density showed a higher association to MRI than Volpara or Quantra density measures. However, classification of women by volumetric density by any of the three mammographic techniques is comparable to classifications by MRI density.”

Average glandular dose in digital mammography and breast tomosynthesis

Olgar T, Kahn T, Gosch D.


SUMMARY OF PUBLICATION:

This study was done to compare the average glandular dose (AGD) in digital full-field mammography (2D imaging mode) and in breast tomosynthesis (3D imaging mode). In order to accurately calculate dose, the researchers of this study chose to use Quantra to estimate glandular tissue content which was used for correction of actual breast composition in each exposure. The conventional 2D mammography and breast tomosynthesis were performed using Hologic’s Selenia® Dimensions® system. Only patients that received both 2D and 3D imaging were included in this study. 2247 conventional 2D mammograms and 984 tomosynthesis images from 641 patients were incorporated in this analysis. The breast glandular tissue content was estimated by the Hologic’s Quantra automated volumetric breast density measurement tool for each patient from Right CC and Left CC images in 2D imaging mode.

The mean percentage volumetric density for this study population estimated by Quantra software was 18.0% and 17.4% for RCC and LCC projections respectively. As a result, calculated mean AGD value based on actual breast glandularities provided by Quantra was higher than those calculated under the assumption of a 50/50 mixture of adipose and glandular tissue. The mean AGD values in 2D imaging mode per exposure after correction for real breast composition were 1.82 mGy and 1.94 mGy for CC and MLO views, respectively; while the same were 2.53 mGy and 2.63 mGy for CC and MLO views, respectively.

The study concludes: “The mean calculated AGD per exposure in 3D imaging mode was on average 34% higher than the 2D imaging mode for patients examined with the same compressed breast thickness. The mean calculated AGDs for both 2D and 3D imaging modes were lower than the dose limits recommended by ACR, European protocols and the diagnostic reference level for Germany.”
Ethnic Variation in Volumetric Breast Density
Sadaf Hashmi, Jamie C. Sergeant, Julie Morris, Sigrid Whiteside, Paula Stavrinos, D. Gareth Evans, Tony Howell, Mary Wilson, Nicky Barr, Caroline Boggis, and Susan B. Astley

SUMMARY OF PUBLICATION:
The authors comment that “The work reported here uses a fully automated, volumetric breast density measure, (Quantra™ software) as opposed to visual assessment or computer assisted methods as reported previously in the literature. Whilst Quantra™ software has not yet been validated with respect to its relationship to risk to the same extent as subjective and area-based methods of density measurement, it holds several advantages over such methods including objectivity, reproducibility, suitability for population-based studies, resolution and the ability to assess absolute, rather than relative, breast density. Regardless of the degree of association with risk, the identification of women with high mammographic density is important because the detection of cancers using conventional mammography is more difficult in this case, and it may be appropriate to use alternative screening methodologies.”

The study concludes: “This study was based on the premise that screening mammography could be made more effective by adapting the imaging modality and the interval to a woman’s individual risk of breast cancer. Breast density plays an important role, not only because it is an important risk factor, but also because it can be altered by lifestyle or other interventions.”

A First Evaluation for Breast Radiological Density Assessment by QUANTRA Software as Compared to Visual Classification
Published: Breast (2012) doi:10.1016/j.breast.2012.01.005

SUMMARY OF PUBLICATION:
Radiologic breast density has been associated with breast cancer risk, and to mammography sensitivity. The method most commonly used for classification is commonly determined on a visual basis. In this study a set of digital mammography exams were classified according to BIRADS quantitative density classification by a panel of experienced radiologists, and by Quantra Breast Density Assessment software. The aim was to compare the two methods.

A set of 418 two view digital mammograms, randomly selected, were used for this study. Visual assessment of breast density was performed independently by 11 radiologists using the BIRADS density categories. The majority report (mode) was used to compare visual to Quantra classification. Intraobserver reproducibility was rather high, with substantial or almost perfect agreement being recorded for 5 or 6 readers.

Although visual classification looks reproducible on a statistical basis, it might have a suboptimal performance when used for a practical purpose. For example, if breast density were to be used as a determinant for a personalized screening protocol, subjects classified as dense by visual classification would range between 25 and 50% according to the study findings.

The author concludes: “Computer assessed breast density is absolutely reproducible, and thus to be preferred to visual classification.”
Racial Differences in Breast Density on Screening Digital Mammograms Comparing R2 Quantra™ Volumetric Computerized Software System vs. Radiologist BIRADS® Density Measures

Richard-Davis G, Lucas L, Disher A, Montgomery-Rice V, Andrade A

Presented: American Society for Reproductive Medicine 67th Annual Meeting; Orlando, FL, USA, October 2011

SUMMARY OF POSTER:

Breast cancer is the second leading cause of death in women. African-American women experience a higher death rate, are more likely premenopausal and triple negative. High mammographic breast density is one of the strongest known risk factors for Breast Cancer with a 4-5X increase. High Breast Density is also associated with 10% to 29% lower sensitivity in radiologist interpretation.

The objective of the study was to 1) compare breast density quantity on digital mammography using radiologist interpretation vs. Quantra computerized software and 2) correlate with race and menopausal status.

Density on digital mammography was not significantly different using BIRADS; 2.25 in Caucasian vs. 2.15 in African American (p= 0.5). BD measured by R2 Quantra volumetric computerized software correlated with interpretation by radiologist. BMI was comparable in Caucasian 31.76 vs. 31.62 in AA (p=0.49).

The study concludes: R2 Quantra and subjective BIRAD readings are associated with each other. This relationship held regardless of race. R2 Quantra density did not differ between premenopausal and menopausal subjects, in contrast to other published data. This pattern also was persistent among racial groups.

Correlation of Ethnicity with Breast Density as Assessed by Quantra™

D. Tzias, S. George, L. Wilkinson, R. Mehta, C. Lobo, A. Hainsworth, A. Sharma

Presented: Royal College of Radiologists Breast Group Annual Scientific Meeting 2011

SUMMARY OF PRESENTATION:

It is widely accepted that there is an association between mammographic density and breast cancer risk. Various studies have examined relationships between ethnicity and breast density patterns using the Wolfe classification system with a view to investigating potential breast cancer risk. Quantra™ is a volumetric assessment tool, which allows reproducible objective measurement of mammographic breast density, eliminating inter-observer variability. This study was designed to investigate the correlation between ethnicity and breast density using Quantra™ measurements.

Quantra values were recorded from mammograms of symptomatic breast patients over a 6 month period. Three different ethnic groups were compared; Black (African and Afro-Carribean), Asian (Indian subcontinent) and White (Caucasian). Mean Quantra™ values were calculated for each group and the Kruskal Wallis test was applied.

The author concludes: “There is a statistically significant difference between the objectively measured breast densities of these three ethnic groups. This is of relevance to the assessment of breast cancer risk.”

A Comparative Study of Volumetric and Area-Based Breast Density Estimation in Digital Mammography:

Results from a Screening Population

Kontos D, Bakic PR, Acciavatti R, Conant EF, Maidment ADA

Published: SPIE Medical Imaging 2010, San Diego, CA, USA

SUMMARY OF POSTER:

This study compared Quantra volumetric breast density with areal breast density in 71 asymptomatic patients with bilateral digital mammography and dynamic contrast MRI studies. Density assessments were done volumetrically (authors' method) on the MRI and both volumetrically and by area (Cumulus) on the digital mammography studies. Results of the three methods were compared. The study found that volumetric density measures from Quantra and MRI were highly correlated; between Quantra and Cumulus the correlation was lower and dependent on the training background of the Cumulus operator. The authors' noted that the absolute values were quite different, with MRI reporting the lowest density values (mean -15%), followed by Quantra (mean -23%) and Cumulus (-29%).

The study concludes: “The strong association with the area-based density measures suggests that [Quantra] volumetric breast density could also potentially be used for breast cancer risk estimation.”
**Investigation of practical scoring methods for breast density**

*Ren B, Smith A, Marshall J*

**Presented:** The 10th International Workshop of Digital Mammography, IWDM 2010, Girona, Catalonia, Spain, June 2010

**SUMMARY OF PRESENTATION:**

This study was conducted to determine if reporting breast density with scoring methods correlated to patient distribution might offer more easily interpretable clinical value. The study consists of 942 patients, acquired from several clinical sites, and with the BI-RADS score available for each patient. The breast density of each mammogram was calculated with Quantra breast density assessment software. In this paper, we describe two new scoring methods for breast density, and evaluate them with a database of 942 patients. Our first method aims to generate a BI-RADS type score to assist doctors to correlate to breast density to BI-RADS category number. The BI-RADS distributions of our database were compared with the population distributions in the ACRIN DMIST [3] study and good agreement was established between the two, suggesting that our database represented a good screening population. With both the breast density and the BI-RADS score results available, we developed two practical scoring methods to generate new quality scores based on breast density results.

The study concludes: Our first method aims to generate a BI-RADS type score to assist doctors to correlate to breast density to BI-RADS category number. The current algorithm has an agreement rate of 62% matching the BI-RADS score from doctors. This performance is similar to how radiologists agree among themselves with BI-RADS scores. Our second method aims to provide statistical information on how a patient's breast density result is compared with a reference population, thus adding insight into the breast density result. Both methods need to be further evaluated to justify them as new methods for breast density.

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**Quantitative Assessment of Breast Density: Comparing of Different Approaches**

*Qin N*

**Presented:** RSNA 2010, Friday, December 3, 2010, 11:00-11:10, Chicago, IL, USA

**SUMMARY OF PRESENTATION:**

The purpose of this study was to compare the numerous approaches to assessing breast density, and to evaluate Quantra’s ability to estimate breast density. Digital mammography studies were performed in the craniocaudal and mediolateral views on 58 patients. Breast density was evaluated by Quantra and human observation methods. Two radiologists estimated breast density using Wolfe classification and BIRADS density scoring. Two radiologists also assessed the breast density in 3D MRI datasets independently. Each assessment method was repeated after two months. Spearman and Pearson correlations of inter-and intra-reader and intermodality density estimates were computed.

The study concludes: High correlation between breast density estimates on R2 Quantra and MRI FCM suggested the former could be used as an effective and accurate application. Quantra automated volumetric breast density measurement may provide an alternative method of determining breast density which has shown to be more accurate and reproducible than other methods.

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**A New Automated Volumetric Breast Density Measurement System Confirms Higher Breast Density Associated with Urban Women**

*Perry N, Milner S, Mokbel K, Duffy S, Pinker K*

**Presented:** European Congress of Radiology 2010, Vienna, Austria

**SUMMARY OF POSTER:**

This study sought to confirm earlier observations that women living in London have higher breast density. The study used Quantra volumetric density assessment, applied to the full-field digital mammograms of 300 women, as the method for measuring volume of fibroglandular tissue, breast volume and the resultant volumetric breast density. The average volumetric density was significantly higher in London before and after adjustment for age. The difference was slightly higher in older women (aged 50 years or more). Neither the breast volume nor volume of fibroglandular tissue correlated to area of residence. London women were significantly more likely to have volumetric density of 25% or higher (p = 0.009).

The study concludes: “Automated volumetric analysis confirms the link between urban and higher breast density, identified by subjective radiologist classification.”
A Comparative Study of Volumetric and Area-Based Breast Density Estimation in Digital Mammography: Results from a Screening Population

Despina Kontos, Predrag R. Bakic, Raymond J. Acciavatti, Emily F. Conant, and Andrew D.A. Maidment


SUMMARY OF PUBLICATION:

This study is a comparison of volumetric versus an area-based breast density estimation method in digital mammography. Volumetric density was measured with Quantra™ (Hologic, Inc.) and area density was estimated using Cumulus (Ver 4.0, Univ. Toronto). Correlation and regression analysis was performed to determine the association between 1) density from left vs. right breasts, and 2) volumetric vs. area based measures.

Bilateral digital mammography images from 71 asymptomatic women were collected and analyzed using Quantra™ volumetric breast density software. The volumetric breast density measures obtained with Quantra™ are strongly correlated, but statistically significantly different that the corresponding area based breast percent density measures obtained with Cumulus. As expected, volumetric density estimates are lower than the corresponding area-based estimates. Both methods were found to be highly consistent.

The author concludes: “The strong correlation observed between right and left breasts indicates that volumetric breast density measures computed by Quantra™ can provide consistent fully-automated measures of breast density for women undergoing mammographic screening.”

Measuring Breast Density Using Quantra™ on Full Field Digital Mammography


Presented: Royal College of Radiology Breast Group 2009, November 2-3 2009, Belfast, UK

SUMMARY OF POSTER:

This study contrasts the numerous approaches to assessing breast composition. It specifically discusses two classes of categorization system based on 1) human observations and 2) human-guided quantitative and automated quantitative measures. The study points out the inter- and intra-reader variability that results from the three most common human observations methods: Wolfe’s classifications categories published in 1976, Boyd’s six-category classification, and BI-RADS. In all three cases a human observer glances at the images and renders a classification based largely on “greyness” of the image, on parenchymal pattern or of the fraction of the area of the breast comprised of parenchymal density. The methods for quantitative analysis are more varied. Interactive thresholding methods such as Cumulus rely on a human operator to adjust a threshold that defines the outline of the parenchymal tissue, the basis of a fractional density measurement by area. Another method utilizes a tissue equivalent phantom within the mammographic image; because the composition of the phantom is understood, comparing pixel values within the phantom with pixel values in the breast tissue can lead to good estimates of the composition of the breast. The third quantitative method, known as SMF, extracts composition data from images, based on its understanding of the physics of the imaging chain; Quantra is a 2nd generation SMF technology.

The study summarizes: “Until now all methods available have been subjective or required manual delineation of tissue outlines. Quantra overcomes these issues and has proved to be such an effective, accurate and efficient application.”
Correlation of Age and HRT with Breast Density as Assessed by Quantra™

Presented: Royal College of Radiology Breast Group 2009, November 2-3 2009, Belfast, UK

SUMMARY OF POSTER:
This study sought to use the Hologic Quantra volumetric breast density tool to remove the impact of intra-observer variability from the consideration of density as a highly significant predictor in the risk of developing breast cancer. In addition, it sought to correct breast density assessment using other methods that do not consider the breast as a 3-dimensional organ. Analysis was performed to correlate Quantra values with variables known to be associated with risk. Under ethics approval, the study observed a population of 320/683 women (47.3%) who responded to a postal questionnaire. Statistical significance was found between Quantra assessments and age, menopausal status, family history and HRT use less than five years. The average volumetric breast density from the studied population was 19%.

The study concludes: “Quantra has shown to be accurate and reproducible by its expected correlation with lifestyle and demographic data. Given its ease of acquisition and display this could be the future of breast density quantification in the digital age.”

Correlation of Age and HRT with Breast Density as Assessed by Quantra™

Presented: RSNA 2009, Monday, November 30 2009, 12:15-13:15, Chicago, IL, USA

SUMMARY OF POSTER:
This study sought to use the Hologic Quantra volumetric breast density tool to remove the impact of intra-observer variability from the consideration of density as a highly significant predictor in the risk of developing breast cancer. In addition, it sought to correct breast density assessment using other methods that do not consider the breast as a 3-dimensional organ. Analysis was performed to correlate Quantra values with variables known to be associated with risk. Under ethics approval, the study observed a population of 320/683 women (47.3%) who responded to a postal questionnaire. Statistical significance was found between Quantra assessments and age, menopausal status, family history and HRT use less than five years. The average volumetric breast density from the studied population was 19%. The study did not demonstrate a significant association between Quantra and ethnicity.

The study concludes: “Quantra could be used to identify women with high density breasts who would benefit from early screening.”

Rafferty E, Smith A, Niklason L

Presented: RSNA 2009, SSM01-04, Wednesday, December 2 2009, 15:30-15:40, Chicago, IL, USA

SUMMARY OF PRESENTATION:
This retrospective study sought to compare three methods of estimating breast density. It compared human assessment from FFDM and tomosynthesis, both using BI-RADS density scoring, and volumetric density from Quantra. 15 radiologists scored the breast density on images from 310 subjects. Images were available for all subjects both for FFDM (Hologic Selenia FFDM system) and breast tomosynthesis (Hologic tomosynthesis prototype). Quantra volumetric breast density was available for 264 subjects. Breast composition was categorized as primarily fatty (BI-RADS 1 or 2) or dense (BI-RADS 3 or 4) by each method for each case and the results compared. The average BI-RADS density scores using FFDM and tomosynthesis were nearly identical, though significant inter-reader variability was observed for both methods. When a volumetric density threshold of 13% was applied to separate dense from fatty cases, comparison showed agreement with radiologists’ BI-RADS scoring in 83% of cases scored as dense and in 87% of cases scored as fatty. The study provides evidence that radiologists’ estimates of breast density scored by the BI-RADS system are similar with FFDM and tomosynthesis, although significant inter-reader variability remains. Computer-based categorization of density also yielded similar density scores while offering the advantage of standardized scoring.

The study concludes: “Volumetric breast density [Quantra] may provide an alternative method of determining breast density.”
Validation of a New Automated Volumetric Breast Density Measurement System as a Marker of Breast Cancer Risk

Pinker K, Perry N, Milner S, Mokbel K, Duffy S

Presented: RSNA 2009, VB31-06, Tuesday, December 1 2009, 10:00-10:10, Chicago, IL, USA

SUMMARY OF PRESENTATION:

This retrospective study sought to validate Quantra’s ability to predict breast cancer risk from full-field digital mammograms. The authors used 200 biopsy-proven breast cancer cases along with 200 age-matched healthy controls. Breast density was measured on the cancer cases by applying Quantra to the contralateral breast. The study demonstrated statistically significant correlation of Quantra results to risk factors such as age. While it did not demonstrate significant association of density with risk, it did show a trend to increased risk with increased dense tissue volume. It also demonstrated significant association of density and risk in women under age 50.

The study concludes: “Quantra automated volumetric breast density measurement is strongly associated with breast cancer risk in women aged under 50, but not in women aged 50 years or over.”

Qualitative and Quantitative Analysis of Fibroglandular Tissue in the Digital Environment


Presented: 10th National Congress of Breast Diseases, Poster 253, 30 Sept – 4 Oct 2009, Izmir, Turkey

SUMMARY OF PRESENTATION:

In this study, 479 cases were evaluated both by Quantra™ and by a human reader. Quantra volumetric density values were divided into four 25% quartiles. The human observer scored each case using the BI-RADS breast tissue composition four-value classification system. The investigators then compared the results for Quantra and the observer. In general, Quantra placed cases into a lower category that did the human observer, indicating a systematic shift between Quantra’s volumetric assessment and the area assessment of a human visual judgment from a 2-D mammogram.

The study concludes: “We believe the relationship between the breast cancer and the fibroglandular tissue density can be evaluated more accurately if the volumetric breast program which provides 3D numerical measurement is used in this assessment.”

Volumetric Assessment of Breast Tissue Composition from FFDM Images


SUMMARY OF POSTER:

This study investigated the stability of a new algorithm to measure volumes within the breast. The algorithm is a refinement of methods published by Highnam and Brady. Two comparisons were performed in this study. The first was a comparison between Quantra™ values measured on FFDM images and values measured through manual segmentation of parenchymal density and breast outline on MR imaging studies for the same women. The second was a comparison of Quantra values measured on left/right and CC/MLO images from the same women. The authors point out that, at the time of this study, “we have not, as yet, explored the relationship between our results and breast cancer risk”.

The study concludes: “Quantra™ has shown to be accurate and reproducible by its expected correlation with lifestyle and demographic data. Given its ease of acquisition and display this could be the future of breast density quantification in the digital age.”