**SSQ01**

**Breast Imaging (Breast Density and Risk Assessment)**

**Scientific Papers**

AMA PRA Category 1 Credits ™: 1.50
ARRT Category A+ Credits: 1.50

Thu, Dec 4 10:30 AM - 12:00 PM  Location: E450A

**Participants**

Moderator
Sughra Raza MD: Consultant, Seno Medical Instruments, Inc
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Stamatia V. Destounis MD: Investigator, FUJIFILM Holdings Corporation Investigator, Seno Medical Instruments, Inc
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Jennifer A. Harvey MD: Researcher, Hologic, Inc Researcher, VuCOMP, Inc Researcher, Volpara Solutions, Ltd Shareholder, Volpara Solutions, Ltd Shareholder, Hologic, Inc

**Sub-Events**

**SSQ01-01**

The Potential Impact of Risk-based Screening Mammography in Women Age 40-49 Years

Elissa Rhona Price MD (Presenter): Nothing to Disclose, Alexander W. Keedy MD: Nothing to Disclose, Rita Gidwaney MD: Nothing to Disclose, Edward A. Sickles MD: Nothing to Disclose, Bonnie N. Joe MD, PhD: Nothing to Disclose

**PURPOSE**

To determine the prevalence of very strong family history and extremely dense tissue in women aged 40-49 with breast cancer detected on screening mammography.

**METHOD AND MATERIALS**

All cancers detected by screening mammography at our institution between 1/1997 and 11/2012 in 40-49 year old women were retrospectively identified. Symptomatic patients undergoing diagnostic mammography and those with a personal history of breast cancer were excluded. Family history, breast density, type of malignancy, tumor receptor status and lymph node status were recorded.

**RESULTS**

During the study period, 194 cases of breast cancer were identified on screening mammography in 40-49 year old women; 53% invasive cancer and 47% ductal carcinoma in situ. Of the patients with invasive disease, 23% had axillary nodal involvement. A very strong family history was absent in 90%, and extremely dense breast tissue was absent in 86%. 78% patients had neither very strong family history nor extremely dense breasts, including 76% of the cases of invasive disease, of which 24% had axillary nodal involvement and 88% had positive hormone receptor status.

**CONCLUSION**

Very strong family history and extremely dense breast tissue were commonly absent in 40-49 year old women with breast cancer detected at screening mammography. Reducing the number of women to be screened in this age group by using a risk-based approach would reduce the number of screen-detected cancers by more than 73%, thereby forgoing most of the benefit of mortality reduction that already has been proven for screening women age 40-49 years.

**CLINICAL RELEVANCE/APPLICATION**

Using a risk-based approach to screening mammography (limiting screening to women with either very strong family history or extremely dense breasts) would reduce by more than 75% the number of screen-detected cancers, thereby forgoing most of the benefit of mortality reduction that already has been proven for screening women age 40-49.

**SSQ01-02**

Impact of State Breast Density Legislation on Primary Care Physicians


**PURPOSE**
A state breast density law, effective April 1, 2013, requires mammography facilities in this state to inform patients if they have dense breasts and to direct them to their primary physicians for questions on breast density and supplemental screening tests. This study investigates primary physician awareness of the law and its impact on outpatient primary care practice and management.

**METHOD AND MATERIALS**

An online survey was distributed to 174 physicians within a large single primary care network system in February 2014, 10 months after a state breast density law took effect. Responses were anonymous. The survey was completed by 77 physicians, 39% from Internal Medicine, 47% from Family Medicine, and 9% from Obstetrics-Gynecology departments. A slight majority (53%) were female. 72% had been practicing for greater than 10 years.

**RESULTS**

49% of respondent physicians were not aware of the Breast Density legislation prior to the survey. 32% reported noticing a change in patient levels of concern about breast density in 2013 compared to prior years. Only 5% of primary physicians were "completely comfortable" answering patient questions about breast density, while 25% were "mostly comfortable". 51% reported themselves as "somewhat comfortable" discussing such questions and 11% were "not comfortable". 48% of respondents reported that they "rarely" answer questions about breast density. Twenty percent of physicians reported they had ordered supplementary screening tests for women with dense breasts who had no other breast cancer risk factors. Of those that ordered additional testing, 44% ordered Breast MRI, 22% ordered whole breast ultrasound, 11% ordered tomosynthesis, and 22% ordered other unspecified testing.

**CONCLUSION**

Nearly half of physicians from one primary care network were not aware of the state's breast density notification law, 10 months after it went into effect. Most were not completely comfortable discussing breast density with patients. Enactment of breast density notification laws without the provision of adequate primary physician education and resources is unlikely to significantly impact patient care.

**CLINICAL RELEVANCE/APPLICATION**

15 states have enacted breast density laws. Physician awareness of the laws and knowledge about breast density are crucial in deciding whether renewal or adoption in additional states is warranted.

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**SSQ01-03**

Automated Volumetric Breast Density and Risk of Cancer Stratified by Pathological Attributes

Stephen W. Duffy: Nothing to Disclose, Oliver William Edmund Morrish MSc: Nothing to Disclose, Lorraine Tucker: Nothing to Disclose, Richard Black MS: Nothing to Disclose, Fiona Jane Gilbert MD (Presenter): Speaker, Bracco Group Research Grant, GlaxoSmithKline plc Research Grant, General Electric Company

**PURPOSE**

To estimate the extent to which automatic measures of density are predictive of breast cancer risk, and in particular risk of the potentially fatal cancers which are prime targets of early detection.

**METHOD AND MATERIALS**

In a retrospective study of breast tomosynthesis in addition to standard full field digital mammography, we had Volpara automated volumetric density on 7019 subjects (1157 cancers) and Quantra automated volumetric density on 7005 subjects (1156 cancers). Data were analysed using logistic regression.

**RESULTS**

These was a significant ($p<0.001$) 3% (95% CI 1-5%) increased risk of breast cancer per 10 cm3 increase in fibroglandular (dense) tissue measured by Volpara, and a significant ($p<0.001$) 2% (95% CI 1-3%) increase per 10 cm3 as measured by Quantra. In both cases, the effect was stronger in invasive grade 3 cancers than in grade 2 or grade 1. Risk of grade 3 breast cancer increased by 4% per 10 cm3 increase in dense tissue measured by Volpara (95% CI 1-7%) and by 3% per 10 cm3 as measured by Quantra (95% CI 1-9%). The effect of neither density measure on risk varied substantially by lymph node status. The effect of Volpara density was considerably stronger for risk of invasive tumours of size greater than 20 mm, at 6% increased risk per 10 cm3 increase dense tissue (95% CI 3-9%). The effect of the Quantra measure had a weaker association with tumour size.

**CONCLUSION**

Automated volumetric breast density is predictive of breast cancer risk. There is evidence that it has stronger predictive power for potentially fatal large and grade 3 invasive cancers. This suggests that automated volumetric breast density has a potential role in risk stratification and management of breast cancer risk.

**CLINICAL RELEVANCE/APPLICATION**

Automated calculation of fibroglandular volume appears to indicate risk of developing breast cancer.

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**SSQ01-04**

Enhanced Personalized Breast Cancer Screening Using an Ensemble Model of Mammographic Texture and Density

Martin Lillholm PhD (Presenter): Employee, Biomediq A/S Shareholder, Biomediq A/S, Joselene Marques

**PURPOSE**

To estimate the extent to which automatic measures of density are predictive of breast cancer risk, and in particular risk of the potentially fatal cancers which are prime targets of early detection.

**METHOD AND MATERIALS**

In a retrospective study of breast tomosynthesis in addition to standard full field digital mammography, we had Volpara automated volumetric density on 7019 subjects (1157 cancers) and Quantra automated volumetric density on 7005 subjects (1156 cancers). Data were analysed using logistic regression.

**RESULTS**

These was a significant ($p<0.001$) 3% (95% CI 1-5%) increased risk of breast cancer per 10 cm3 increase in fibroglandular (dense) tissue measured by Volpara, and a significant ($p<0.001$) 2% (95% CI 1-3%) increase per 10 cm3 as measured by Quantra. In both cases, the effect was stronger in invasive grade 3 cancers than in grade 2 or grade 1. Risk of grade 3 breast cancer increased by 4% per 10 cm3 increase in dense tissue measured by Volpara (95% CI 1-7%) and by 3% per 10 cm3 as measured by Quantra (95% CI 1-9%). The effect of neither density measure on risk varied substantially by lymph node status. The effect of Volpara density was considerably stronger for risk of invasive tumours of size greater than 20 mm, at 6% increased risk per 10 cm3 increase dense tissue (95% CI 3-9%). The effect of the Quantra measure had a weaker association with tumour size.

**CONCLUSION**

Automated volumetric breast density is predictive of breast cancer risk. There is evidence that it has stronger predictive power for potentially fatal large and grade 3 invasive cancers. This suggests that automated volumetric breast density has a potential role in risk stratification and management of breast cancer risk.

**CLINICAL RELEVANCE/APPLICATION**

Automated calculation of fibroglandular volume appears to indicate risk of developing breast cancer.
PURPOSE

Mammographic Density (MD) is scientifically well established as an independent breast cancer risk factor and is increasingly used in clinical practice for personalized screening. Mammographic parenchymal patterns/textures beyond MD is known to provide further risk segregation. We investigate the risk segregation potential of an ensemble of mammographic density and texture measures from FFDM.

METHOD AND MATERIALS

A case/control study was selected from the Dutch Breast Cancer Screening program. Mammograms were acquired on a Hologic Selina FFDM system with a 70μm pixel size. 250 screen detected cancer cases were chosen randomly and likewise for 750 cancer-free controls. Cases were represented by the latest cancer-free prior contralateral MLO view (if available) and otherwise by the contralateral MLO view at time of diagnosis. Controls were represented by the latest available MLO view (laterality matched individually per case).

Volumetric density was calculated using Volpara 1.45. Based on a large literature review (e.g. Giger, Manduca, Höberle, Heine), a total of 56 measures of mammographic texture were implemented and measured for each mammogram. Furthermore, a novel machine learning based texture measure was trained on an independent training set and measured on each mammogram. A multivariate logistic regression model for all 58 measured (and linearly age-corrected) markers was 5-fold cross-validated and evaluated for association to cancer outcome through AUC.

RESULTS

In total, 28 of the age-corrected markers resulted in AUCs significantly better than chance. Specifically, the novel machine learning based measure resulted in an AUC of 0.65 (95% CIs 0.61-0.69) whereas volumetric density was non-significant (AUC 0.51). The multivariate logistic regression yielded a pooled AUC across the five folds of 0.75 (0.71-0.79).

CONCLUSION

By combining a representative range of published mammographic texture measures with a novel machine learning based approach, it was possible to separate future cancer cases from healthy controls to a degree that a) clearly improves on what is attainable through density alone and b) could facilitate personalized screening of, e.g., high risk women.

CLINICAL RELEVANCE/APPLICATION

Clinical practice includes screening based on, e.g., age and family history through risk models as Gail and Tyrer-Cuzick. Such models could be enhanced by texture measures from routine mammograms.

Comparing Breast Density Measurement Techniques in Screening Digital Mammography

Oliver William Edmund Morrish MSc (Presenter): Nothing to Disclose, Lorraine Tucker: Nothing to Disclose, Richard Black MS: Nothing to Disclose, Stephen W. Duffy: Nothing to Disclose, Fiona Jane Gilbert MD: Speaker, Bracco Group Research Grant, GlaxoSmithKline plc Research Grant, General Electric Company

PURPOSE

To compare different methods of assessing breast density in a UK screening population.

METHOD AND MATERIALS

Conventional two-view digital mammograms were collected from six centres from 8867 women attending either a screening assessment clinic, or screening for family history. Breast density was assessed by 26 experienced image readers on a visual analogue scale and by two automated volumetric density tools (QuantraTM, Hologic and VolparaTM, Matakina). Total breast volume, fibroglandular volume and percent volume density for each view were combined logically to produce results for each woman.

RESULTS

There was a good linear correlation (R2=0.95) between Quantra and Volpara for total breast volume with a mean difference of 43.5cm3 (5.04% of the mean result ±0.32%, 2sem). There was less correlation for fibroglandular volume (R2=0.74) and the mean difference was 30.3cm3 (21.19%±0.72%). On average Quantra gave the larger value and the difference tended to increase with increased volume. For the percent volume density the mean difference was 1.61% (16.32%±0.69%) and R2 was 0.65. Comparison of the observer’s scores with the area-based Quantra density yielded a poor correlation (R2=0.31). Exponential correlations of observer's scores with the volumetric density results gave R2 values of 0.33 and 0.38 for Quantra and Volpara respectively.

CONCLUSION

There is poor correlation of breast density scored by observers and automated techniques. In part this may be explained by differences in the quality being measured (area vs volume) and image presentation (for presentation vs for processing). However inter-observer variability in the UK may be high as quantitative estimations of breast density are not made routinely. If automated methods are to be used differences in their output, caused by differences in the underlying algorithm, need to be understood.

CLINICAL RELEVANCE/APPLICATION
There are differences in the results of each of the breast density measurement methods. These differences need to be understood if management decisions are based on breast density.

**SSQ01-06**

*The Diagnostic Effect of Digital Breast Tomosynthesis in Relation to Visually Assessed and Automated Volumetric Breast Density*

Stephen W. Duffy: Nothing to Disclose, Oliver William Edmund Morrish MSc: Nothing to Disclose, Lorraine Tucker: Nothing to Disclose, Richard Black MS: Nothing to Disclose, Fiona Jane Gilbert MD (Presenter): Speaker, Bracco Group Research Grant, GlaxoSmithKline plc Research Grant, General Electric Company

**PURPOSE**

To assess the benefit in terms of diagnostic accuracy of addition of digital breast tomosynthesis (DBT) by breast density, as measured on a visual analogue scale and by automated volumetric software.

**METHOD AND MATERIALS**

In a retrospective study of DBT in addition to standard full field digital mammography, we had visually assessed density on 6969 subjects (1153 cancers), Volpara automated volumetric density on 7019 subjects (1157 cancers) and Quantra automated volumetric density on 7005 subjects (1156 cancers). All subjects had mammography by 2D digital mammography alone and by 2D digital mammography plus DBT. Sensitivity and specificity was compared for between 2D mammography alone and 2D plus DBT using McNemar methods.

**RESULTS**

Median and interquartile ranges were 38% (23-50%) for visually assessed percent density, 72 cm3 (51-103) for absolute dense volume as measured by Volpara and 93 cm3 (51-143) for absolute dense volume measured by Quantra. Specificity was significantly improved with the addition of DBT in all tumours and in all subgroups as defined by breast density (p<0.001 in all cases). Sensitivity was improved significantly (p=0.03) with the addition of DBT in those subjects with visual density at or above the 3rd quartile (50%), with 86% sensitivity (95% CI 82-90%) for 2D mammography alone and 93% (95% CI 90-96%) for 2D mammography plus DBT. A significantly improved sensitivity (p=0.02) was also observed for those at or above the third quartile of Volpara density (103 cm3) Volpara, with a sensitivity of 87% (95% CI 83-91) for 2D mammography alone and 93% (95% CI 90-96%) for 2D mammography plus DBT. No significant difference in sensitivity was observed for those with high density as measured by Quantra, and no significant difference was observed for those with low density as measured by any of the three methods.

**CONCLUSION**

DBT has the potential to improve sensitivity of mammography in women with dense breast tissue.

**CLINICAL RELEVANCE/APPLICATION**

In women with more than 50% breast density, the addition of DBT may increase cancer detection.

**SSQ01-07**

*Quantitative Background Parenchymal Enhancement in Breast DCE-MRI Is Associated with Breast Cancer Risk*


**PURPOSE**

Visually estimated background parenchymal enhancement (BPE) by BI-RADS categories in breast dynamic contrast enhanced MRI (DCE-MRI) has been correlated with breast cancer risk in high-risk women. We tested this association using fully automated, objectively derived, quantitative BPE measurements.

**METHOD AND MATERIALS**

A retrospective case-control study was performed using breast DCE-MRI scans from 102 patients (mean 47.2±7.3 YO) who underwent either open surgical biopsy or core biopsy from 2009-2011: 51 women had unilateral breast cancer and 51 were age- and date-of-MRI matched controls with a unilateral biopsy-proven benign. The MRI was analyzed using fully automated computer algorithms, generating two quantitative BPE measures computed from the third post-contrast series: the absolute BPE volume ([BPE]) and its relative amount over the whole breast volume (BPE%). Breast density BI-RADS was retrieved from the mammography report (< 6 months) prior to diagnosis. Volumetric absolute and relative amounts of fibroglandular tissue ([FGT] and FG T%) were also automatically quantified from the MRI. Multivariable conditional logistic regression was performed to assess BPE measures as predictors of breast cancer risk: (comparison 1) breasts contralateral to the cancers vs. benign breasts of the controls, and (comparison 2) breasts contralateral to the cancers vs. contralateral (negative) breasts of the controls.

**RESULTS**

After adjustment for breast density, [FGT], and FG T%, odds ratio (OR) for comparison 1 was 1.84 (95%
Confidence interval [CI]: 1.08, 3.14; p=0.02) for |BPE| and 3.85 (95% CI: 1.34, 11.05; p=0.01) for BPE%. OR for comparison 2 was 1.71 (95% CI: 1.08, 2.71; p=0.02) for |BPE| and 2.30 (95% CI: 1.15, 4.59; p= 0.02) for BPE%. OR for breast density alone was 0.75 (95% CI: 0.35, 1.59; p=0.5). For comparison 1, OR was 1.19 (95% CI: 0.71, 1.97; p=0.5) for |FGT|, and 0.71 (95% CI: 0.19, 2.67; p=0.6) for FGT%; for comparison 2, OR was 1.14 (95% CI: 0.72, 1.81; p=0.6) for |FGT|, and 0.70 (95% CI: 0.19, 2.52; p=0.6) for FGT%.

CONCLUSION

Increased BPE (both |BPE| and BPE%) in breast DCE-MRI are predictive of breast cancer risk, independent of measures of breast density and FGT.

CLINICAL RELEVANCE/APPLICATION

Objectively quantified BPE in breast DCE-MRI has potential for use as a biomarker of breast cancer risk and may be included to improve breast cancer risk assessment and stratification.

SSQ01-08

Imaging Biomarkers of Breast Cancer Risk: Does MRI Background Parenchymal Enhancement Increase the Likelihood of Breast Cancer in High Risk Women?

Brian Nicholas Dontchos MD (Presenter): Nothing to Disclose, Habib Rahbar MD: Nothing to Disclose, Savannah Corrina Partridge PhD: Nothing to Disclose, Larissa Korde MD, MPH: Nothing to Disclose, Sue Peacock MSC: Nothing to Disclose, Constanze D. Lehman MD, PhD: Consultant, Bayer AG Consultant, General Electric Company Research Grant, General Electric Company

PURPOSE

Imaging assessments of amounts of fibroglandular tissue are known markers of breast cancer risk. Variable levels of enhancement of normal breast tissue on MRI (background parenchymal enhancement [BPE]) also may be predictive of breast cancer development. We explored whether BPE can further refine breast cancer risk assessments beyond mammographic density and amount of fibroglandular tissue on MRI in high risk women.

METHOD AND MATERIALS

After IRB approval, we identified all high risk screening MRIs at our institution from 1/2006 to 12/2011 in women ≥18 years with no history of breast cancer. Outcomes were determined from our regional tumor registry. Women diagnosed with breast cancer any time after the index MRI comprised the cancer cohort. A 1:1 case control was created from a randomized cohort of women who did not develop breast cancer by last follow-up (minimum 3 years after index MRI), matching for age and BRCA mutation, and maximizing follow-up time. BPE, amount of fibroglandular tissue on MRI, and mammographic density were assessed on index exams and compared between the cancer cohort and negative controls using conditional logistic regression analyses.

RESULTS

From 5333 exams during the study interval, 23 high risk women (6 BRCA mutations) with no history of breast cancer underwent screening MRI and were subsequently diagnosed with breast cancer during the follow up interval (12 invasive, 11 in situ). Cancer cohort mean age was 47 ±10 years. Mean time-to-diagnosis of cancer was 779 ± 600 days, and mean follow-up time for negative controls was 2037 ± 458 days. Women with mild, moderate, or marked BPE on their index MRI had an approximately 9 times greater risk of cancer diagnosis during the follow-up interval than those with minimal BPE (OR=9.0, CI: 1.1-71.0). Neither amount of fibroglandular tissue on MRI nor mammographic density was a significant predictor of cancer risk (OR=1.2, CI: 0.4-3.9; OR=1.4, CI: 0.4-4.4, respectively).

CONCLUSION

Increased BPE may be associated with a higher probability of developing breast cancer in high risk women. Amounts of fibroglandular tissue measured by mammography or MRI may be less predictive of future breast cancer diagnosis in the high risk population.

CLINICAL RELEVANCE/APPLICATION

Increasing background parenchymal enhancement on MRI correlated with future breast cancer development among high risk women and could be used as a predictive biomarker of breast cancer risk.

SSQ01-09

Contrast Enhancement Kinetics Quantified in Breast DCE-MRI and Breast Cancer Risk


PURPOSE

Contrast enhancement kinetics derived from breast dynamic contrast enhanced MRI (DCE-MRI) has been shown to have diagnostic value. We investigated the relationship between objectively quantified kinetic parameters in DCE-MRI and breast cancer risk.

METHOD AND MATERIALS
A retrospective case-control study was performed based on a group of 102 women (mean 47.2±7.3 YO) who underwent breast biopsies from 2009-2011: 51 women had unilateral breast cancer and 51 were age- and date-of-MRI matched controls with a unilateral biopsy-proven benign. BI-RADS-based mammographic breast density was retrieved from the latest (< 6 months) mammography report prior to diagnosis. The breast MRI at time of diagnosis (cancer or benign) was analyzed on the normal breast contralateral to cancer (for cancer cases) or benign (for controls). The region of the fibroglandular tissue (FGT) was estimated in the MRI for each analyzed breast using a fully automated computer algorithm. Based on the enhancement time-signal intensity curves of three DCE post-contrast series, four kinetic parameters, i.e., peak enhancement, time to peak enhancement, wash-in-slope, and wash-out-slope were quantified for each voxel specifically over the estimated FGT region; mean and variance of the voxel-wise values of each of the four kinetic parameters were then computed, generating a total of 8 kinetic measures. We compared these kinetic measures between the normal breasts contralateral to the cancers and the contralateral (negative) breasts of the controls. Multivariable conditional logistic regression was performed to estimate odd ratios (ORs) for breast cancer.

RESULTS

After adjustment for breast density and the amount of FGT, the OR for mean wash-in-slope was 1.12 (95% Confidence Interval (CI): 1.01, 1.25; p=0.04) and 1.81 (95% CI: 1.13, 2.91; p=0.01) for the variance of wash-in-slope. Variance remained significant (OR was 1.80 [95% CI: 1.07, 3.03; p=0.03]), even after additional adjustment for quantitative measures of background parenchymal enhancement (BPE). The ORs for all other 6 kinetic measures were not statistically significant.

CONCLUSION

The mean and variance of wash-in-slope in breast DCE-MRI are associated with breast cancer risk.

CLINICAL RELEVANCE/APPLICATION

The kinetic parameters of wash-in-slope quantified in breast DCE-MRI show potential as biomarkers of breast cancer risk and may be included to potentially improve breast cancer risk prediction.