Discordant Interpretation of Screen-Detected Cancers Using Tomosynthesis and Independent Double Reading in a Population-Based Mammography Screening Program

**Participants**
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**Sub-Events**

**SSA01-01**

**Title:** Discordant Interpretation of Screen-Detected Cancers Using Tomosynthesis and Independent Double Reading in a Population-Based Mammography Screening Program

**Participants**
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**Purpose**
Analyze missed screening cancers (SDC) with tomosynthesis (DBT) using independent double reading in population-based screening

**Method and Materials**
Trial was approved by Ethical Committee. Participating women signed a written consent. 24,301 women age 50-69 undergoing FFDM+DBT were included. The trial had 4 arms: A=FFDM,B=FFDM+CAD,C=FFDM+DBT, D=syn2D+DBT. Reading was performed in batch mode using a 5-point rating scale. 8 readers participated alternating between reading modes. Scores 1 (neg) and 2-5 (pos) were stored directly into the national screening database. Cases with positive score by at least one reader were discussed at arbitration meeting before final decision for recall. There was automated recording of all reading times directly into the screening database. Cases of discordant cancers were mainly the two arms C-D including DBT were analyzed.

**Results**
230 SDC were diagnosed: 3 cancers in arm A+B only, 172 cancers in both main arms A+B and C+D, and 55 cancers in arm C+D only (detection rate 2D=175 or 7.2/1000 vs. 2D+3D=227 or 9.3/1000, p<0.001). Among SDC in both main arms, discordant rate (cancer missed by one reader) was 50/172 (29%) for arms A-B and 41/172 (24%) for arms C-D. Discordant rate for DBT-only was 30/55 (55%). Discordant cancers for arms C-D among the 172 SDC included spiculated mass or distortion in 17/41 (41%) and in 21/30 (70%) for DBT-only cases. Discordance for microcalc's only was 16/41 (39%) and 2/30 (7%), respectively. Median reading time for exams with negative score by all 4 readers (n=20,106) was: Arm A 25 sec, arm B 28 sec, arm C 62 sec (range 36-170), and arm D 58 sec (range 36-156). For the 55 DBT-only detected cancers, median reading time for TP's in arm C-D was 229 and 217 sec compared with 70 and 59 sec for FN's, respectively. 4/6 (67%) of SDC among the 30 discordant DBT-only cancers with less than 45 sec reading time presented as spiculated mass or distortion. The TP rate (detected cancers among all read) for arms C-D for individual readers varied from 7% to 39%. The radiologist with shortest reading time missed most cancers.

**Conclusion**
Discordant interpretation is a challenge in screening including use of DBT, and subtle cancers presenting as spiculations might easily be missed at DBT using batch reading

**Clinical Relevance/Application**
Subtle cancers manifesting with spiculations might easily be overlooked. Training and careful reading might reduce number of missed small cancers

**SSA01-02**

**Title:** Breast Density Comparison Between Synthesized Versus Full Field Digital Mammography

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**Purpose**
Analyze and compare breast density between synthesized and full field digital mammography.

**Method and Materials**
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Maryam Rezvani, MD, Salt Lake City, UT (Abstract Co-Author) Nothing to Disclose
Nan Hu, PhD, MS, Salt Lake City, UT (Abstract Co-Author) Nothing to Disclose
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PURPOSE
To evaluate perceptual difference in breast density classification using synthesized mammography (SM) compared to full field digital mammography (FFDM) for screening mammography.

METHOD AND MATERIALS
This institutional review board approved retrospective multi-reader study evaluated breast density on 200 patients who underwent baseline screening mammogram during which both SM and FFDM were obtained from 6/1/2016 through 11/30/2016. Qualitative breast density was independently assigned by 7 readers (blinded to each other) initially viewing FFDM alone. Then, in a separate session, these readers assigned breast density using synthetic views alone on the same 200 patients and were again blinded to each other's assignment. Qualitative density assessment was based on Breast Imaging Reporting and Data Systems (BI-RADS) 5th Edition. Generalized linear mixed effects model (GLMEM) was used to evaluate the association of breast density between SM and FFDM taking into account random variation by controlling for age and breast thickness on breast density classification and readers. Odds ratios (ORs) and their 95% confidence intervals (CIs) were then calculated for these variables.

RESULTS
The OR for denser breast classification in SM versus FFDM was 0.581 (95% CI: 0.460, 0.733; p-value < 0.0001) demonstrating a statistically significant denser breast assignment on SM compared to FFDM per patient across the readers. Raw data analysis shows 81.8% had no change in density assignment between SM and FFDM, 6.3% were higher density in FFDM though 11.9% had a higher density assigned in SM. The OR for compressed breast thickness was 1.26 (p=0.01) reflecting generally lower density in thicker breasts. The OR for age was 1.47 (p-value < 0.001) reflecting higher density BI-RADS classification in younger women.

CONCLUSION
SM is associated with a higher qualitative breast density BI-RADS assessment compared to FFDM resulting in a higher likelihood of assigning a greater density classification in SM compared to FFDM.

CLINICAL RELEVANCE/APPLICATION
Synthesized mammography (SM) is increasingly replacing full field digital mammography (FFDM), but its impact on qualitative breast density classification has not been studied. Density assessment is important as it conveys information regarding cancer risk and accuracy of mammography, which may alter decisions about adjunctive imaging, therefore determining whether assessment differs between SM and FFDM is important.

Honored Educators
Presenters or authors on this event have been recognized as RSNA Honored Educators for participating in multiple qualifying educational activities. Honored Educators are invested in furthering the profession of radiology by delivering high-quality educational content in their field of study. Learn how you can become an honored educator by visiting the website at: https://www.rsna.org/Honored-Educator-Award/ Maryam Rezvani, MD - 2015 Honored Educator

SSA01-03 The Relationship between Quantitative Breast Density, Age and Cancer Detection Rate in a Large UK Breast Screening Population

Sunday, Nov. 26 11:05AM - 11:15AM Room: Arie Crown Theater

Awards
Student Travel Stipend Award

Participants
Sam Dumonteil, MBBS, FRCR, London, United Kingdom (Presenter) Nothing to Disclose
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PURPOSE
Quantitative breast density has been proposed as one of the most promising variables to stratify screening strategies; however, little is known about the relationship between density and cancer detection rates (CDR), which we evaluate in a prospectively collected cohort of patients in a UK breast screening program.

METHOD AND MATERIALS
We included 70,435 consecutive screening digital mammograms for women age 47-73 performed between March 2013 and September 2016. We excluded women at high risk as defined by National Health Service Breast Screening Programme (NHSBSP) protocols. Breast density was quantitatively measured using Volpara density software (VolparaSolutions, Edition 5 Wellington, NZ) and categorised by Volpara Density Grade (VDG). We divided our population into three 9 year age groups, 47-55, 56-64 & 65-73 in
order to compare CDR in the lowest (VDG 1) and highest (VDG 4) density women stratified by age. Differences in CDR by density group in each tertile were tested using Fisher's exact test with p<0.05 to signify statistical significance.

RESULTS
A total of 70,435 screening mammograms in 63,577 women were included revealing 557 cancers for an overall CDR of 0.8%. In 47-55 year olds, women in the VDG 1 density group had a CDR of 0.16%; women in the VDG 4 density group had a CDR of 0.85%. The difference of 0.69% was statistically significant (p=0.01). In 56-64 year olds, women in the VDG 1 density group had a CDR of 0.63%; women in the VDG 4 density group had a CDR of 0.58%. The difference of 0.04% was not statistically significant (p=0.84). In 65-73 year olds, women in the VDG 1 density group had a CDR of 0.99%; women in the VDG 4 density group had a CDR of 0.24%. The difference of 0.75% was statistically significant (p=0.04).

CONCLUSION
We found an opposite trend between breast density and CDR between the youngest and oldest age groups. Older women with the least dense breasts had a higher CDR than those with the densest breasts while the reverse was true in younger women. The differences in CDR between the densest and least dense women were statistically significant in the youngest and oldest age groups.

CLINICAL RELEVANCE/APPLICATION
The relationship between cancer detection rate and density may vary with age and should be taken into account when stratifying women into different screening strategies based on density.

Participants
Yi-Chen Lai, MD, Taipei, Taiwan (Presenter) Nothing to Disclose
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PURPOSE
To compare the performance of two-dimensional synthetic mammography (SM) in combination with digital breast tomosynthesis (DBT) versus conventional full-field-digital mammography (FFDM) in the detection of microcalcifications on screening examinations.

METHOD AND MATERIALS
In this HIPAA-compliant, IRB-approved protocol, a multi-reader (n=4), retrospective observer study was conducted. Seventy-two consecutive screening mammograms performed with FFDM, digital breast tomosynthesis (DBT), and SM, which were recalled for calcifications from 2014-2015, constituted the study dataset. There were 54 benign and 18 malignant calcification cases. Twenty normal control screening mammograms without calcifications were also included. All normal or benign cases were verified with at least 1-year follow-up and suspicious lesions verified with biopsy. Two anonymized datasets were created, one consisting of FFDM images and another consisting of SM and DBT images. Two readers reviewed each anonymized dataset. Calcification recalls were tabulated. Sensitivity and specificity for calcification detection were calculated and compared for the SM+DBT versus FFDM group. A mixed effects generalized linear model was used to account for correlation between multiple interpretations of the same image.

RESULTS
Reader agreement for FFDM was 82.6% (95%CI, 73.3%-89.7%), Cohen's kappa = 0.733, p<0.001 and for SM+DBT was 79.3% (95%CI, 69.6%-89.1%), Cohen's kappa = 0.677, p<0.001. Overall sensitivities for benign and malignant calcification detection were 77.8% and 94.4%, respectively, for FFDM versus 59.3% and 88.9%, respectively, for SM+DBT. Specificity was 100% for FFDM and 97.5% for SM+DBT. There were no statistically significant differences in either sensitivity or specificity between the study groups (p>0.89).

CONCLUSION
Relative to FFDM, SM in combination with DBT demonstrated a trend towards lower sensitivity for the detection of calcifications on screening examinations, although this did not reach statistical significance. There was no significant difference in specificity between the study groups. Further investigation with a larger dataset is ongoing.

CLINICAL RELEVANCE/APPLICATION
Relative to FFDM, SM in combination with DBT may have reduced sensitivity for the detection of calcifications, and therefore continued acquisition of FFDM images for screening examinations may be warranted.

Participants
Maryam Etesami, MD, New Haven, CT (Presenter) Nothing to Disclose
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SSA01-05 Cancer Detection with Digital Breast Tomosynthesis (DBT) Compared with Conventional Digital Mammography in Routine Breast Cancer Screening

Sunday, Nov. 26 11:25AM - 11:35AM Room: Arie Crown Theater

Participants
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preventive tests. Women with false positive screening mammogram results were no less likely to have a subsequent pap smear and bone mass testing also supported the positive association between breast cancer screening and subsequent uptake of preventive services in the Medicare population, including pap smears, bone mass measurement, and influenza vaccinations.

METHOD AND MATERIALS

This was a retrospective institutional review board approved, HIPAA compliant study with waiver of informed consent. DM screening mammograms performed from August 1, 2008 through August 1, 2011 and DBT screening mammograms performed from August 1, 2011 through August 1, 2016 at an academic center were reviewed. DBT screening mammogram was offered to all patients after installation. Cancer detection rates were calculated and compared between the DM and DBT screening mammograms. Histological type of detected cancers, their size, receptor phenotype and lymph node status based on sentinel axillary lymph node biopsy were compared between the 2 groups of DBT and DM only screening.

RESULTS

This study included a total of 44050 screening mammograms, 28282 (64%) DBT and 15768 (36%) DM only. The cancer detection rate was 5.41 per 1000 patients screened with DBT and 4.95 per 1000 patients screened with DM only (p=0.52). There was no significant difference in proportions of in situ and invasive cancers detected (67% and 70% invasive cancers with DBT and DM only, respectively. p=0.55). However, the cancers detected with DBT were significantly smaller (1.54 ± 1.4 cm) compared with cancers detected with DM only (2.30 ± 2.3 cm) (p=0.01). Additionally, axillary lymph node metastasis in invasive cancers was reduced to approximately half with DBT screening (14.7%) compared to DM only screening (30.9%) (p=0.03). DBT screening detected more invasive cancers with lobular histology (13%) compared with DM only (7%), but the difference was not statistically significant (p=0.29). There was no significant difference in receptor phenotype of the cancers detected by DBT compared to DM only screening.

CONCLUSION

DBT screening detects smaller cancers with fewer positive axillary lymph nodes compared to DM. This difference may translate to less systemic treatment and improved clinical outcomes.

CLINICAL RELEVANCE/APPLICATION

DBT screening may improve breast cancer early detection compared to DM which may lead to less systemic treatment and improved clinical outcomes

SSA01-06 Association of Breast Cancer Screening Utilization and Results with Uptake of Subsequent Preventive Services

Sunday, Nov. 26 11:35AM - 11:45AM Room: Arie Crown Theater

Participants
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PURPOSE

To assess for potential associations between screening mammography use and subsequent uptake of a variety of preventive services in the Medicare population, including pap smears, bone mass testing, and influenza vaccinations.

METHOD AND MATERIALS

Medicare claims from 2010-2014 Research Identifiable Files were used retrospectively to identify a group of women who underwent screening mammography and a control group without screening mammography in 2012. The screened group was divided into positive versus negative screening results, with the positive subgroup further divided into false positive and true positive findings. Bivariate and multivariate logistic regression models were used to examine the relationship between screening status and the probabilities of receiving a pap smear, bone mass measurement, or influenza vaccine in the subsequent two years. Sensitivity analysis was performed using a 2-year clean period for pap smear and bone mass testing prior to mammography for assessment of subsequent preventive service uptake.

RESULTS

The cohort consisted of 555,708 patients, 66.6% without screening mammography and 31.4% with mammography. After adjusting for patient demographics, comorbidity status, geographic covariates, and baseline preventive care, women who underwent an index screening mammogram (with either positive or negative results) were more likely than unscreened women to have a subsequent pap smear, bone mass measurement, and influenza vaccine (OR 1.52-2.75). Sensitivity analysis with a 2-year clean period for prior pap smear or bone mass testing also supported the positive association between breast cancer screening and subsequent uptake of preventive tests. Women with false positive screening mammogram results were no less likely to have a subsequent pap smear and
CONCLUSION
In female Medicare beneficiaries, screening mammography utilization is associated with higher likelihood of adherence to other preventive guidelines, and without a negative association between false positive results and near-term cervical cancer or osteoporosis screening. Potential effects of mammography on attitudes toward preventive testing merit further investigation.

CLINICAL RELEVANCE/APPLICATION
False positive mammograms do not deter women from undergoing cervical cancer or osteoporosis screening. Screening mammography use was associated with improved subsequent uptake of preventive tests.

SSA01-07 Unique Mammographically-Derived Compositional Signatures of Malignancy and Triple-Negative Breast Cancers

Sunday, Nov. 26 11:45AM - 12:05PM Room: Arie Crown Theater

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PURPOSE
To investigate the unique lipid, water, and protein composition of malignant breast cancers by receptor status to non-malignant breast tissue in a cohort of high risk women (BIRADS 4 or greater).

METHOD AND MATERIALS
A dual-energy mammography technique (3CB) was used to quantify lipid, protein, and water composition. The lesion dataset included malignant (invasive and DCIS, N=86) and non-malignant (fibroadenoma and benign, N=282) groups. The malignant group contained 10 triple-negative and 34 receptor-positive invasive cancers. Within regions identified by the radiologists, water, lipid, and protein measures were generated and within three surrounding rings of 2 mm thicknesses. Differences and ratios between lesions and rings were also calculated. Logistic regression with cross validation was applied to analyze lesion type separation.

RESULTS
The most significant variables to discriminate malignancy were lipid differences between lesion and rings (p-value (p) =10E-5, odds ratio (OR)=0.57), protein (water) difference between lesion and rings (p=10E-4, OR=1.66), and ratios of lesion water to rings (p=10E-5, OR=1.79). At the same time, the most significant variables of triple-negative and receptor-positive discrimination were lipid difference (negative) between ring 1 and ring 3 (p=0.03, OR=0.24 (0.065, 0.86)) and the increasing lipid levels (slope) from inner to outer ring (p=0.07, OR=2.44 (0.92, 6.5)). Thus, the lipid content within the lesion relative to the surrounding rings is a marker of malignancy, but the steeper lipid gradient outside of the lesion is a marker of triple-negative breast cancer.

CONCLUSION
We found biologically meaningful water, lipid, and protein compositions of lesion and its periphery that are statistically significant for malignancy/non-malignancy and triple-negative/receptor-positive separation. In addition, future studies will determine if the lipid gradient surrounding the lesion is indicative of active lipolysis within adjacent mammary adipocytes. If true, this advanced mammography imaging technique could aid in selecting patients that benefit from inhibition of this lipolysis.

CLINICAL RELEVANCE/APPLICATION
Advanced dual-energy mammography may reduce unnecessary biopsies and better select women with invasive cancer by receptor status.

SSA01-08 Breast Cancer Detection Rate of Supplemental Screening with Abbreviated MR for Women with Dense Breasts: Preliminary Results

Sunday, Nov. 26 11:55AM - 12:05PM Room: Arie Crown Theater

Participants
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Dense breast tissue decreases the sensitivity of mammography and many women with dense breasts are requesting supplemental screening such as whole breast ultrasound. At our institution we offer an abbreviated Breast MRI (AB-MR) examination as an option for women seeking supplemental screening. In this study, we evaluate the early outcomes of our AB-MR examination in asymptomatic women with dense breast tissue and negative recent mammography.

METHOD AND MATERIALS
An IRB approved and HIPAA compliant retrospective review was performed of women with who underwent supplemental screening with AB-MR examination. All women were asymptomatic. Their most recent mammogram was negative or benign (BI-RADS 1 or 2) and rated as "dense" (heterogeneous or extreme). The cancer detection and false positive rates were calculated based on pathologic correlation.

RESULTS
86 women underwent supplemental screening with AB-MR from January 2016 to April 2017. The age ranged from 41 to 76 years, mean 56 years. Four patients (4.6%) were categorized as BI-RADS category 4. Pathology results revealed 1 invasive ductal carcinoma, 1 invasive lobular carcinoma, 1 radial scar, and 1 case of fibrocystic change. The supplemental cancer detection rate with AB-MR was 2/86 or estimated to 23 per thousand with 2 false positive exams.

CONCLUSION
Given the additional cancer detection during our early implementation of AB-MR screening, the examination appears very promising as a supplemental screening tool in women with dense breasts. However, more data is needed for validation.

CLINICAL RELEVANCE/APPLICATION
Our preliminary results suggest that the AB-MR may have a role as a supplemental screening option for women with dense breast tissue.

Three-dimensional functional infrared imaging (3DIRI) based on multiparametric evaluation of metabolic imaging biomarkers, shows promise as an indicator for the risk of a current breast cancer in women with dense breasts. Women with positive 3DIRI result (high risk) were recommended to undergo adjuvant contrast-enhanced screening MRI. The objective of this study was to assess and compare, in a retrospective reader study, radiologists' performance in detection of breast cancer using 2D digital mammography alone and using 2D digital mammography with 3DIRI.

METHOD AND MATERIALS
In this retrospective, multicase, sequential-design reader study, 10 radiologists, with varying mammography experience, interpreted a cancer-enriched set of 2D mammography and 3DIRI examinations. All imaging studies were of asymptomatic women with either heterogeneous or extremely dense breasts. Observers first interpreted the 2D mammogram alone and subsequently combined with the 3DIRI cancer risk result presented as a range of -100 to +100 with numbers in the negative range indicating, in a non-ordinal manner: "no risk" for current malignancy, to +100 for "risk of current malignancy". Radiologists rated examinations using forced BI-RADS categories 1-5 and probability of malignancy on a 100 point scale with 0 as "no possibility of malignancy present" and 100 as "malignancy present". The analysis included 40 cases: 30 noncancers and 10 histology confirmed cancer cases. Reader performance was compared using the receiver operating characteristics (ROC) curve and the area under the curve (AUC) for mammography alone and for mammography with 3DIRI.

RESULTS
Multi-reader pooled ROC analysis yielded AUC of 0.71 for mammography alone and 0.87 for mammography with 3DIRI, yielding a statistically significant 22% relative increase in AUC (change in AUC of 0.16 [95% confidence interval: 0.04-0.27]; p < 0.05).

CONCLUSION
Adding 3DIRI to mammography significantly improved reader’s detection of breast cancer in women with dense breast tissue.

CLINICAL RELEVANCE/APPLICATION
3D functional infrared imaging, a non-contract, non-radiation imaging modality, can correctly classify women for their current risk of breast cancer with high efficacy. Assessing the likelihood for breast cancer non-invasively can assist in risk-stratified screening programs.