SSQ02-01 • Computer Derived Texture Features on DCE-MRI Can Separate ER+ Breast Cancers with Low and High Oncotype DX Scores

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PURPOSE
Oncotype DX (ODX) is a gene-expression based assay for predicting response to hormonal therapy in estrogen receptor positive (ER+) breast cancers (BCa) patients. The goal of this study was to identify whether computer derived texture features on DCE-MRI can distinguish low and high ODX scores (i.e. ER+ BCa patients who would and would not benefit from adjuvant chemotherapy), thereby providing a non-invasive pertherapeutic gene-expression assessment tool predicting tumor treatment response.

METHOD AND MATERIALS
A total of 57 ER+ BCa patient studies were collected, in which 21 breast MRIs were acquired from a Phillips 1.5T magnet with a 7-channel breast coil, and 36 MRIs were acquired using a Siemens 1.5T magnet with a 8-channel breast coil, including DCE images obtained prior to, during, and after administration of 0.1 mmol/kg of Gd-DTPA. Each study was accompanied by: i) lesion annotations from an expert radiologist; and ii) ODX scores. A set of 6 morphological features, 3 pharmacokinetic features, 12 enhancement kinetic features (EKF), 12 intensity kinetic features, 312 textural kinetic features, 6 dynamic local binary patterns (DLBP), and 5 dynamic histogram of oriented gradients (DHoG) features were extracted and used to characterize the appearance of the breast lesions. The computed features were evaluated by a linear discriminate analysis (LDA) classifier in terms of their ability to distinguish ER+ BCa with low or high ODX scores via a 2-fold randomized cross validation scheme.

RESULTS
The DHoG, DLBP, and EKF texture features yielded AUC values of 0.85, 0.82, and 0.80 in conjunction with the 2-class LDA classifier for separating low and high ODX ER+ breast lesions.

CONCLUSION
This work to our best knowledge, the first attempt to quantitatively correlate texture measurements on DCE-MRI to patient outcome prediction via the ODX assay. Our results suggested that the DHoG, DLBP, and EKF were robust and stable DCE-MRI markers in distinguishing between low and high ODX scores.

CLINICAL RELEVANCE/APPLICATION
An MRI-based assay to identify ER+ BCa patients that could non-invasively predict which patients would benefit from adjuvant chemotherapy, and could serve as a complement to Oncotype DX assay.
Hui Li PhD (Presenter) ; Maryellen L Giger PhD * ; Li Lan ; Sunny Y Duan ; Stephan Hu ; Gillian M Newstead MD * ; Hiroyuki Abe MD ; Michelle Lindgren MD

PURPOSE
To investigate the potential usefulness of quantitative imaging analysis on characterizing both mass and non-mass-like enhancement breast lesions in the task of distinguishing between malignant and benign lesions.

METHOD AND MATERIALS
Study was performed on 123 biopsy-proven lesions from 103 MRI studies acquired between January 2009 and April 2010, including 35 benign mass, 50 malignant mass, 11 benign non-mass-like and 27 malignant non-mass-like lesions. Our quantitative imaging analysis method incorporated computerized 3D lesion segmentation and feature extraction, including kinetic, enhancement-variance kinetic, morphological, size, and texture features. Output from the system yielded the probability of malignancy from a Bayesian artificial neural network (BANN). Classification performance was evaluated with a leave-one-case-out method using ROC analysis with area under the ROC curve as the figure of merit.

RESULTS
For mass lesions, the kinetic features of time to peak and curve shape index statistically differed between malignant and benign lesions. However, kinetic features did not contribute significantly in the diagnostic task with non-mass-like breast lesions. By merging computer-selected features with BANN classifiers, AUC values of 0.88 (SE=0.03), 0.95 (SE=0.02), and 0.82 (SE=0.08) were obtained in the task of distinguishing between malignant and benign lesions on the entire dataset, between malignant and benign mass lesions, and between malignant and benign non-mass-like lesions, respectively.

CONCLUSION
Kinetic characteristics are useful in differentiating malignant from benign mass lesions; however, their performance is reduced when the lesions are non-mass-like. Thus, quantitative analysis for diagnostic decision-making should be performed separately on mass and non-mass-like lesions.

CLINICAL RELEVANCE/APPLICATION
In order to improve clinical diagnostic accuracy, quantitative analysis for diagnostic decision-making should be performed separately on mass and non-mass-like lesions in the classification task.

SSQ02-03 • Use of Quantitative 3D Breast Image Analysis to Inform DCIS Staging

Stephanie M Burda (Presenter) ; Maryellen L Giger PhD * ; Li Lan ; Kathy Rodogiannis ; Hui Li PhD ; Gillian M Newstead MD * ; Ken Yamaguichi ; Koichi Ishiyama MD ; Hiroyuki Abe MD ; Michelle Lindgren MD ; Adam Starkey

PURPOSE
Uncertainty on which ductal carcinoma in situ (DCIS) cases will progress to invasive breast cancer currently results in overtreatment. Our purpose was to discern quantitative characteristics of pure DCIS, DCIS with an invasive component, and invasive cancers without DCIS to inform prognosis of patients with lesions presenting initially as DCIS.

METHOD AND MATERIALS
Retrospective, IRB-approved review of our radiology database 2005-2012 identified 303 pathology-proven cancers with correlative MR imaging. Histology yielded 54 pure DCIS lesions, 56 with both DCIS and invasive pathology, and 193 invasive cancers without DCIS. Quantitative 3D image analysis yielded morphological, kinetic, and texture lesion descriptors following semi-automated lesion segmentation. ROC analysis was performed on these image-based phenotypes comparing pure DCIS lesions, DCIS lesions with an invasive component and invasive cancers without an in situ component.

RESULTS
The combination of features that best distinguished pure DCIS from invasive cancer included kinetic feature time to peak, texture features of contrast and correlation, and morphological features of circularity, margin, and surface area. The combination of features that was best able to distinguish pure DCIS from invasive cancers with a DCIS component included contrast, margin, and ratio of surface area to volume. The margin characteristics (determined by spiculation and sharpness) and contrast (the difference between the average gray level of the cancer and the surrounding area) were found to be insightful in both comparisons. Time to peak was also significant in the comparison of Pure DCIS and invasive cancers, yielding an AUC value of 0.77. Round-robin evaluation of an LDA yielded AUCs of 0.85 and 0.74 distinguishing pure DCIS from invasive cancers and invasive cancers with a DCIS component, respectively.

CONCLUSION
Image-derived quantitative phenotypes, which indicate a likelihood of invasive disease of pure DCIS, could patient guide management of DCIS lesions, thus potentially reducing overtreatment.

CLINICAL RELEVANCE/APPLICATION
Image-derived quantitative phenotypes, which indicate a likelihood of invasive disease of pure DCIS, could patient guide management of DCIS lesions, thus potentially reducing overtreatment.

SSQ02-04 • Undetected Breast Cancers on Commercial Breast MRI CAD (Computer-aided Detection) System
Chae Hyun Kim; Seon Hyeong Choi (Presenter); Ji Yeon Park; Yoonjung Choi MD; Shin Ho Kook MD

PURPOSE
To evaluate the immuno-histological factors of breast cancer not detected on breast MRI CAD system.

METHOD AND MATERIALS
The study included 327 preoperative breasts MRI of histologically proven breast cancer from July 2011 to February 2013. We retrospectively reviewed the MRI CAD results, corresponding immune-histopathologic features, lesion size and age to determine factors affecting MRI CAD detectability. We categorized tumors into two groups: detected and undetected groups.

RESULTS
Of the 327 cases, the CAD system marked 259 (79.2%) lesions correctly and 68(20.8%) were undetected on breast MRI CAD. The mean size and age were 18 mm (range:1-70) and 50.0 yo (SD:9.9) in the undetected group and 22.8 mm (range: 3-120) and 51.4 yo (SD: 10.7) in the detected group. Detectability rates for IDCs, DCIS were 86.7% (208 of 240) and 44.6% (25 of 56), respectively. The tumor type was a significant (p

CONCLUSION
Though the commercial breast MRI CAD system showed good performance, about 20% of breast cancers were not detected on MRI CAD. DCIS, low nuclear grade, low Ki-76 percentage, and HER-2 negative influenced the breast MRI CAD detectability in breast cancer patients.

CLINICAL RELEVANCE/APPLICATION
DCIS, low nuclear grade, low Ki-67, and HER-2 negative can influence CAD detectability. So, radiologist should check immunohistologic profiles and original images when interpreting breast MRI CAD.

SSQ02-05 • Immunohistological Factors Affecting the Breast Cancer Size Measurement by MRI Computer-aided Detection (CAD) System
Ji Yeon Park; Seon Hyeong Choi (Presenter); Yoonjung Choi MD; Chae Hyun Kim; Shin Ho Kook MD

PURPOSE
To investigate immunohistological factors affecting the breast tumor size measurement discrepancy between the MRI CAD and the pathologic specimen.
METHOD AND MATERIALS
We retrospectively reviewed the 244 cases of breast MRI CAD images and pathologic findings of the 244 patients who underwent operation for breast cancer between July 2011 and December 2012. We compared the CAD generated tumor size with tumor size measured on pathologic specimen. We classified the tumors into three groups: underestimated, adequately measured and overestimated group. We investigated the statistical difference in histopathology including histologic type, presence of DCIS, extensive intraductal component, nuclear grade, ER, PR and HER-2, among the 3 groups.

RESULTS
Median tumor size on CAD and specimen were 20 mm (2-163 mm) and 17 mm (0.8-82 mm), respectively. Adequately measured group was 68.6% (n=168). Invasive ductal carcinoma (IDC) showed significantly more adequate measurement, compared with DCIS (p=0.025). Among IDC, the presence of extensive intraductal component was significantly higher in overestimated group (p

CONCLUSION
Size assessment using breast MRI CAD was accurately measured in 68.6%. On MR CAD, breast cancer size was frequently overestimated in cases of DCIS, the presence of extensive intraductal component, and HER-2(+).

CLINICAL RELEVANCE/APPLICATION
Accurate tumor size measurement is critical to surgical plan for breast conservation.
Size assessment by breast MRI CAD is accurate but it can be overestimated in cases of DCIS, EIC, and HER-2(+).

SSQ02-06 • Quantitative MRI-based Phenotypes of Triple Negative Breast Cancers
Hui Li PhD (Presenter) ; Maryellen L Giger PhD * ; Li Lan ; Hiroyuki Abe MD ; Michelle Lindgren MD ; Eric M Blaschke MD ; Gillian M Newstead MD *

PURPOSE
To investigate the potential usefulness of quantitative image analysis on characterizing the molecular subtypes of breast cancer in order to better understand the difference between triple negative and other molecular subtypes of breast cancer

METHOD AND MATERIALS
Study was performed on 168 biopsy-proven breast cancer MRI studies acquired between November 2008 and August 2011, in which 40 cases were triple negative (ER-, PR-, and HER2-) breast cancers and 128 cases were of other molecular subtypes including Luminal A, Luminal B, and HER2. Quantitative MRI analysis included: 1) 3D lesion segmentation based on a fuzzy c-means clustering algorithm; 2) computerized feature extraction; 3) leave-one-out linear stepwise feature selection; and 4) discriminant score estimation using Linear Discriminant Analysis (LDA). The classification performance between triple negative and other molecular subtypes of breast cancer was evaluated using ROC analysis with area under the ROC curve (AUC) as the figure of merit.

RESULTS
The triple negative classification, in a round-robin evaluation, yielded AUC values of 0.90 (SE=0.05) and 0.67 (SE=0.05) on 3T and 1.5T MR scanners, respectively, in the task of distinguishing between triple negative and other molecular subtypes, statistically significantly higher than an AUC value of 0.5 (p-value

CONCLUSION
The results from this study indicate that quantitative MRI analysis shows promise in the discrimination of triple negative breast cancer from other molecular subtypes of breast cancer.

CLINICAL RELEVANCE/APPLICATION
Identification of the molecular subtypes of breast tumors is expected to allow for improved prognostic assessment and more effective cancer treatment plans.
Mirinae Seo MD (Presenter) ; Nariya Cho MD ; Min Sun Bae MD, PhD ; Eun Bi Ryu MD ; Jung Min Chang MD ; Hye Ryong Koo MD ; Su Hyun Lee MD ; Won Hwa Kim MD, MS ; Woo Kyung Moon ; Hye Mi Gweon MD ; A Jung Chu MD

PURPOSE
To evaluate the features of undiagnosed cancers at prior screening breast MRIs in patients who subsequently developed breast cancers and the potential utility and limitation of computer-aided evaluation (CAE).

METHOD AND MATERIALS
Between March 2004 and March 2013, 65 pairs of dynamic contrast enhanced breast MRIs including prior negative screening MRIs and subsequent MRIs with developed cancers (mean interval 36.5 months, range 5.4 – 96.7 months) were identified. The mean histological sizes of developed cancers was 2.0cm (range 0.5 - 9.5 cm) for invasive cancers (n=44) and 1.9cm (range 0.5 - 4.1 cm) for DCIS (n=21). Visible findings, their maximum lesion size and actionability, as well as causes for overlooked cancers on prior MRI were determined and classified by two experienced radiologists in consensus. A commercially available CAE program was retrospectively applied to the prior MRIs with visible findings for generation of kinetic features including washout, plateau, and persistent enhancement proportions. Presence of a washout component on CAE was also described.

RESULTS
Of the 65 areas where cancer later developed, 51% (33 of 65) of prior MRIs had visible findings and their mean lesion size was 1.0cm (range 0.4 - 5.2 cm). Of these visible findings, 24% (8 of 33) were classified as actionable and 76% (25 of 33) as underthreshold. Causes for actionable findings were mimicking of physiologic enhancement (n=3), mismanagement after benign results of biopsy (n=3), and satisfaction of search (n=2). Those of underthreshold findings were small lesion size (n=6), moderate to marked background parenchymal enhancement (n=11), mimicking of post-op scar (n=7), and peripheral location (n=1). Twenty three of the visible findings were available for CAE and the washout component was found in 14. However, 4 of 14 lesions with a washout component were not marked due to marked background enhancement with multiple enhancing lesions with a washout component. CAE did not show the washout component in 9 of 23 lesions.

CONCLUSION
On prior screening breast MRIs in which cancer later developed, 51% (33 of 65) had visible findings (24% actionable, 76% underthreshold). The addition of CAE has the potential to identify 43% (10 of 23) of overlooked findings. Yet, there are still some limitations on CAE.

CLINICAL RELEVANCE/APPLICATION
When an enhancing lesion shows a washout component on MR-CAE of screening breast MRI, closer attention is warranted.

Lia Morra PhD * ; Silvano Agliozzo PhD * ; Luca A Carbonaro MD * ; Manuela Durando (Presenter) ; Barbara Pesce MD ; Giovanna Mariscotti ; Alberto Bert PhD *

PURPOSE
To evaluate the performance of a commercial computer aided detection (CAD) system (CAD BREAST DTS, Im3D S.p.A.) for detecting lesions at digital breast tomosynthesis (DBT) on an independent testing set.

METHOD AND MATERIALS
The CAD system was retrospectively tested on a set of 143 patients. Craniocaudal (CC) and mediolateral oblique (MLO) DBT projections were acquired with a Hologic Selenia Dimensions system and reconstructed.
with the Briona library (Real Time Tomography LLC). All patients signed an informed consent form. A total of 80 histologically confirmed malignant lesions (57 masses, 18 microcalcification clusters and 6 masses with associated microcalcifications) were detected and annotated by experienced radiologists who drew a 3D bounding box around each lesion view. CAD BREAST DTS yields both masses and microcalcification clusters candidates. For masses, a CAD true positive was registered when the CAD marking overlapped by at least 20% the radiologists marking; for microcalcification clusters, when at least two of the microcalcifications identified by CAD fell within the radiologists marking. A CAD false positive was registered in all other cases, to avoid chance matchings. Masses with associated microcalcifications were considered correctly identified if CAD marked at least a mass or a microcalcification cluster.

RESULTS
At the selected operating point, per-lesion sensitivity was 89% (95% C.I. 80-94%). The system detected 48/56 masses, 17/18 microcalcification clusters and 6/6 masses with microcalcifications. Mean number of false positives per view was 2.8 ± 1.9 (mean ±standard deviation), of which 2 were marked as masses and 0.8 as microcalcification clusters.

CONCLUSION
The DBT CAD sensitivity is comparable to that observed for 2D digital mammography CAD systems, with a fairly low number of false positives per view. Further work, especially on difficult cases such as screening interval cancers, and comparing reading with and without CAD, is needed to understand its role in clinical practice.

CLINICAL RELEVANCE/APPLICATION
A commercial CAD system for masses and microcalcification clusters detection is evaluated on an independent testing set.

SSQ02-09 • Quantitative MRI Morphological Features of Breast Cancer: Correlation with Immunohistochemical Biomarkers and Subtypes

Min Sun Bae MD, PhD (Presenter) ; Mirinae Seo MD ; Woo Kyung Moon ; Nariya Cho MD ; Jung Min Chang MD ; Hye Ryoung Koo MD ; Won Hwa Kim MD, MS ; Su Hyun Lee MD ; Hye Mi Gweon MD

PURPOSE
To investigate the correlation of the tumor roundness measured quantitatively at contrast-enhanced magnetic resonance imaging (MRI) and immunohistochemical biomarkers and subtypes in breast cancer.

METHOD AND MATERIALS
After IRB approval, we retrospectively reviewed 280 consecutive women (median age, 50 years; range, 28-79 years) with 282 invasive breast cancers (< 5 cm size). All patients underwent preoperative breast MRI. Images were assessed independently by the two radiologists who were unaware of pathological findings. Tumor roundness was measured quantitatively by a software developed in-house and was calculated according to the following equation: roundness = 4? x A / P2 (A is the cross-sectional area of the tumor and P is the measured perimeter length of the tumor). The means of values measured by the two observers were recorded and interobserver variability was calculated. Associations between the tumor roundness (1-100 %) and biomarker (estrogen receptor [ER], progesterone receptor [PR], HER2, and Ki67) features were evaluated using Pearson’s correlation coefficient and a multiple linear regression analysis. Tumor roundness was compared between breast cancer subtypes (luminal A, luminal B, HER2-enriched, and triple-negative).

RESULTS
Interobserver agreement for MRI measurements was moderate with intraclass correlation coefficients of 0.75 (95% confidence interval: 0.67-0.80). A moderate inverse correlation was observed between the ER score and tumor roundness (-0.408, P < .0001). PR score, Ki67 index, and tumor grade correlated with the tumor roundness (P < .0001). In multiple linear regression, ER score (P < .0001) and Ki67 index (P = .003) were independent factors determining tumor roundness. Triple-negative tumors showed the highest mean roundness score compared with other subtypes (67.3 for triple-negative vs. 55.9 for HER2-enriched, 53.8 for luminal B,
and 51.7 for luminal A; P < .0001).

CONCLUSION
Tumor roundness measured quantitatively at MRI correlated with ER score and Ki67 index in breast cancer. Triple-negative tumors showed the highest mean roundness score compared with other subtypes.

CLINICAL RELEVANCE/APPLICATION
Our data may have implications for possibly stratifying breast cancer patients with different clinical outcomes by using MRI morphological features.