Evaluation of Benign and High-Risk, Nonmalignant Breast Lesions, assessed as False-Positive at Contrast-Enhanced (CE) MRI using DW imaging and CE MR Imaging Features

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TARGET AUDIENCE: This study could be relevant to oncologists, researchers, or breast radiologists.

PURPOSE: To evaluate the diffusion weighted (DW) imaging (DWI) characteristics of nonmalignant lesion subtypes and classify them using apparent diffusion coefficient (ADC), morphological and texture-based image features derived from contrast enhanced (CE) MRI.

METHODS: This HIPPA-compliant retrospective study was IRB approved with a waiver of consent. Lesions were assessed as BIRADS 4 or 5 at MRI, subsequently proved to be nonmalignant at biopsy using histology as a reference standard. These patients underwent 3.0T MRI with DWI (b=0, 600 s/mm^2) from 2008 to 2012 for pre-operative staging of recently proven breast cancer or high-risk screening. Axial DWI used single-shot dual spin-echo sequence with EPI readout. Sagittal T1-weighted CE-MR images were acquired using the VIBRANT gradient echo before and at three points at 60-s intervals after an injection of 0.1 mmol/kg of gadopentetate dimeglumine. Patients who received neoadjuvant chemotherapy prior to MRI were excluded. Patients with a lesion size less than 0.8 cm or DW images with artifacts or poor fat suppression were also excluded. The ADC was calculated using Functools software by selecting a region of interest (ROI) within the lesion. Haralick texture image features [1] were extracted from ROI encompassing the enhanced area of lesion on post-contrast T1 MR Image that was segmented using ITK-SNAP software. Nonmalignant lesions were classified as high risk (HR) and other benign group. A nonparametric Wilcoxon rank sum test and a Chi-square test were used to determine the statistical significance to differentiate HR lesions from other benign lesions using ADC values and image-based texture parameters. To assess the power of the predictors in differentiating between the high risk and the low risk benign groups, logistic regression analysis (2) as well as the area under the receiver operating characteristic (ROC) curve (AUC) was employed. Statistical significance was established at $p < 0.05$. The ADC unit is 10^{-3}mm/s.

Table 1: The ADC values of non-malignant breast lesions

	High-Risk Lesions (n = 23)		Benign Lesions (n = 95)	
Value	n.lesions	ADC(mean±SD)	n.lesions	ADC(mean±SD)
Menopause status				
Premenopausal	7	1.300±0.181	56	1.600±0.251
Postmenopausal	16	1.400±0.370	39	1.600±0.223
Breast Density (group)				
Fatty (0)	1	0.810±0.000	4	1.500±0.188
Scattered dense (1)	5	1.200±0.179	15	1.500±0.169
Heterogeneously dense (2)	15	1.400±0.349	49	1.600±0.226
Extremely dense (3)	2	1.300±0.092	27	1.600±0.284
Background enhancement (group)				
Minimal (0)	5	1.400±0.367	28	1.700±0.298
Mild (1)	3	1.200±0.778	25	1.600±0.258
Moderate (2)	9	1.300±0.196	33	1.500±0.161
Marked (3)	6	1.300±0.171	9	1.500±0.171

RESULTS: A total of 118 lesions (23 high risk and 95 benign) in 111 women (median age: 47.5 yrs; range 23-81 years) were included in the study. Our hypothesis was that the discriminative power between groups can be improved to a greater extent by using imaging features as compared to using the ADC feature alone. For the candidate features, we performed Wilcoxon rank sum test to investigate whether significant difference existed between the two groups. The most significant variable was ADC with p=0.0003 (**Fig 1-Left**)). For menopause status, breast density, and background enhancement, the difference of ADC between the HR group and other benign lesions group is described in **Table. 1**.

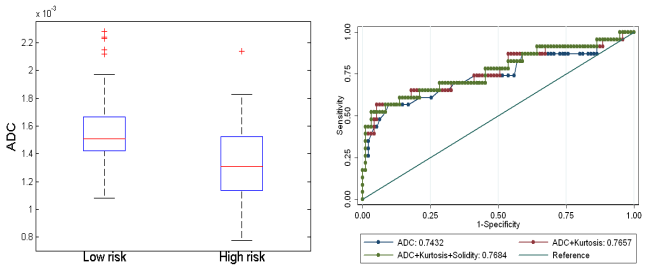

Fig 1: (Left) Box plot shows the comparison of ADC values of high risk and benign breast lesions. Benign lesions had significantly high ADC value ($p < 0.001$) than high-risk lesions. (Right)ROC curves for different models in differentiating the high risk benign group from the other low risk benign group.

Among the clinical variables, age and menopausal status showed statistical significance with p=0.0104 and 0.0145, respectively. Kurtosis and solidity were the imaging features that showed statistical significance with p=0.0181 and 0.044, respectively. A Chi-square test was performed to assess potential differences between the two groups in dichotomous variables: menopausal status (premenopausal vs. postmenopausal), breast density (0,1 vs. 2,3), and background parenchymal enhancement (BPE) (0,1 vs. 2,3); resulting in p=0.0139, 0.5215, and 0.0705, respectively. A model with ADC alone showed AUC=0.743. When ADC and kurtosis were used, the performance was slightly better, resulting in AUC=0.766 (**Fig 1-Right**)). However, the inclusion of solidity to the model with ADC and kurtosis did not yield any further improvement (AUC=0.768).

DISCUSSION AND CONCLUSION: There is only one study that investigated the potential of ADC to differentiate HR lesions from other benign lesions (3). The study done at 1.5T suggested that HR lesions had significantly lower ADC values than other benign lesions. Our study is the first one that uses 3.0T MRI data and explores the potential impact of ADC in conjunction with image-based features. Our analysis confirmed that lower ADC values may correlate with the high-risk nature of the breast lesion. Usually, high-risk lesions found on imaging require complete surgical excision as a small percentage of them turn out to be cancer at surgery. Such procedures are expensive, provoke anxiety and cause morbidity. Therefore, the ability to identify HR lesions from the other benign lesions may avoid unnecessary biopsies of benign lesions especially those that are not associated with cancer.

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