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Brief Communications

Breast density quantitative measures and breast cancer risk among screened Black women

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Abstract

Mammographic density is a strong predictor of breast cancer but only slightly increased the discriminatory ability of existing risk prediction models in previous studies with limited racial diversity. We assessed discrimination and calibration of models consisting of the Breast Cancer Risk Assessment Tool (BCRAT), Breast Imaging-Reporting and Data System density and quantitative density measures. Patients were followed up from the date of first screening mammogram until invasive breast cancer diagnosis or 5-year follow-up. Areas under the curve for White women stayed consistently around 0.59 for all models, whereas the area under the curve increased slightly from 0.60 to 0.62 when adding dense area and area percent density to the BCRAT model for Black women. All women saw underprediction in all models, with Black women having less underprediction. Adding quantitative density to the BCRAT did not statistically significantly improve prediction for White or Black women. Future studies should evaluate whether volumetric breast density improves risk prediction.

Mammographic density (MD) is a strong predictor of breast cancer, but it has been shown to increase the discriminatory ability of existing risk prediction models only slightly (1). Previous studies found that adding MD to the Breast Cancer Risk Assessment Tool (BCRAT, Gail model) increased the C-statistic by only 0.01-0.06 units (2,3). These previous studies had limited racial diversity. Our group has developed automated quantitative methods to measure breast density directly from images, and we demonstrated that Black women had lower Breast Imaging-Reporting and Data System (BI-RADS) breast density assignments, despite having a greater quantity of dense breast tissue compared with White women when quantitative measures were used (5). This study evaluated whether quantitative MD measures improve the predictive accuracy of the BCRAT model for White and Black women.

Details of the study population and data collection are reported elsewhere (6) and will be made fully available at the time of publication. Women screened with full-field digital mammography or a combination of full-field digital mammography and digital breast tomosynthesis at the Hospital of the University of Pennsylvania between September 1, 2010, and December 31, 2014, were included. Dense area and area percent breast density measurements were obtained using the fully automated, validated LIBRA software (7). Among 17 380 women with available breast images, we selected the first image and excluded screening exams with uncertain outcomes (n = 13), people with a prior history of breast cancer (n = 74), true-positive and false-negative screening exams (n = 153), women with breast implants (n = 429), and non-White or non-Black women (n = 1649). Patients were followed up from the date of first screening mammogram until invasive breast cancer diagnosis or 5-year follow-up through December 31, 2019, and 5-year risk estimates were calculated using the BCRAT (BCRA R package [v2.1] https://dceg.cancer.gov/tools/risk-assessment/bcra). Women with ductal carcinoma in situ were considered noncases because the Gail model predicts invasive cancers. We calculated performance measures, and McCarthy et al. (2021) explains in detail how the performance measures of calibration and discrimination were characterized as well as the methods used to calculate the respective 95% confidence intervals (CIs). We assessed discrimination using the area under the curve (AUC) and calibration using the observed to expected ratio and 95% confidence intervals as previously described (6). We assessed the following models: BCRAT alone, BCRAT + BI-RADS density, BCRAT + quantitative density measures, and BCRAT + BI-RADS density + quantitative density measures. As a sensitivity analysis, BMI was added to each of the models for women with BMI values.

Table 1 displays characteristics of the study population for Black (n = 10 064, 59%) and White (n = 6881, 41%) women. Black women had greater breast area and dense area but lower percent density compared with White women. Model performance stratified by race or ethnicity is displayed in Table 2. AUCs for White women stayed consistent approximately 0.59 for all models, whereas the AUCs increased slightly from 0.60 (95% CI = 0.56 to 0.64) to 0.62 (95% CI = 0.60 to 0.64) when adding dense area and

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Table 1. Characteristics of cancer patients by race

Risk factors	White (n = 6881)	Black (n = 10 064)
No. (%)[a]	6881 (41%)	10 064 (59%)
Cancers detected, no. (%)	123 (2%)	123 (1%)
Cancer subtypes, no. (%)[b]		
ER/PR+HER−	97 (78%)	83 (67%)
ER/PR+HER+	8 (7%)	12 (10%)
ER/PR-HER+	7 (6%)	5 (4%)
ER/PR-HER−	5 (4%)	19 (15%)
Invasive missing	6 (5%)	4 (3%)
Age, mean (SD), y	57 (10)	56 (11)
Age category, no. (%), y		
40-49	1897 (28%)	3173 (32%)
50-59	2322 (34%)	3345 (33%)
60-69	1879 (27%)	2288 (23%)
70+	783 (11%)	1258 (13%)
BMI, no. (%), kg/m^2[c]		
<25	3146 (46%)	1372 (14%)
25-29.9	1864 (27%)	2562 (25%)
30+	1596 (23%)	5674 (56%)
Missing	275 (4%)	456 (5%)
Age at menarche, no. (%), y		
<12	1164 (17%)	2122 (21%)
12 to 13	3708 (54%)	4347 (43%)
≥14	1524 (22%)	2234 (22%)
Missing	485 (7%)	1361 (14%)
Age at first birth, no. (%)		
Nulliparous	2030 (30%)	1491 (15%)
<20 y	286 (4%)	3530 (35%)
20-24 y	1074 (16%)	2495 (25%)
25-29 y	1733 (25%)	1268 (13%)
≥30 y	1594 (23%)	647 (6%)
Missing	164 (2%)	633 (6%)
Prior breast biopsy, no. (%)		
None	4994 (73%)	8184 (81%)
One	1415 (21%)	1485 (15%)
Two or more	472 (6%)	395 (4%)
Prior atypical hyperplasia/benign breast findings, no. (%)	108 (2%)	26 (0.3%)
No. of first-degree relatives with breast cancer, no. (%)		
None	5456 (79%)	8768 (87%)
One	1292 (19%)	1141 (11%)
Two or more	133 (2%)	155 (2%)
BI-RADS density, no.[a] (%)[d]		
Almost entirely fatty	508 (7%)	1804 (18%)
Scattered fibroglandular tissue	3651 (53%)	6037 (60%)
Heterogeneously dense	2522 (36%)	2107 (21%)
Extremely dense	188 (3%)	91 (1%)
Missing	12 (1%)	25 (0.2%)
Breast area, mean (SD), cm^2	150 (65)	207 (82)
Percent breast density, mean (SD), %	18 (12)	14 (11)
Dense breast area, mean (SD), cm^2	23 (18)	26 (28)

[a] Percentage of total women in the population.
[b] Percentage of total invasive cancers.
[c] Body Mass Index.
[d] Breast Imaging-Reporting and Data System.

area percent density to the BCRAT model for Black women. Both Black and White women saw underprediction of breast cancers in all models, with Black women having less underprediction. Underprediction of the BCRAT model was reduced when adding dense area and area percent density from 1.25 (95% CI = 0.89 to 1.38) to 1.18 (95% CI = 0.90 to 1.30) in White women. Underprediction of the models stayed relatively the same, with an observed to expected ratio ratio 1.10 for Black women even when adding both quantitative MD measures. Prediction was not meaningfully improved when the results were stratified by family history, menopausal status, or age nor when BMI was added to the models for both Black and White women.

Adding quantitative mammographic density to the BCRAT did not significantly improve predictive accuracy for White or Black women. AUC remains approximately 0.59 for White women and 0.62 for Black women in all models, with no statistically significant differences in AUCs by race or when density measures were added to the BCRAT. Underprediction is worse in White women than in Black women.

This study is the first, to our knowledge, to examine if adding quantitative mammographic density improves breast cancer risk prediction for Black women alone. The lack of significant improvement of the predictive accuracy for both White and Black women could be attributed to several reasons. There was a relatively low number of invasive breast cancer cases among Black or White women in the cohort. This study used 2-dimensional (2D) images to calculate area breast density. Digital breast tomosynthesis is rapidly expanding, which enables 3-dimensional estimation of breast density, which has been shown to be even more strongly associated with breast cancer risk than 2D breast density

Table 2. Performance of absolute risk models by race or ethnicity[a,b]

	White		Black	
	AUC (95% CI)	O/E (95% CI)	AUC (95% CI)	O/E (95% CI)
Absolute risk (BCRAT)	0.59 (0.56 to 0.60)	1.25 (0.89 to 1.38)	0.60 (0.56 to 0.64)	1.10 (0.90 to 1.25)
Absolute risk + BI-RADS density	0.59 (0.57 to 0.59)	1.21 (0.88 to 1.30)	0.61 (0.59 to 0.63)	1.10 (0.92 to 1.24)
Absolute risk + dense area	0.59 (0.58 to 0.60)	1.22 (0.95 to 1.30)	0.62 (0.60 to 0.64)	1.02 (0.88 to 1.15)
Absolute risk + percent density	0.59 (0.58 to 0.60)	1.20 (0.90 to 1.28)	0.62 (0.60 to 0.64)	1.10 (0.98 to 1.19)
BI-RADS + dense area	0.59 (0.59 to 0.62)	1.21 (0.91 to 1.29)	0.61 (0.60 to 0.64)	1.10 (0.92 to 1.20)
BI-RADS + percent density	0.60 (0.59 to 0.62)	1.19 (0.91 to 1.29)	0.62 (0.60 to 0.64)	1.12 (0.94 to 1.23)
Absolute risk (BCRAT) + BMI	0.60 (0.59 to 0.61)	1.20 (0.93 to 1.31)	0.61 (0.59 to 0.62)	1.10 (0.98 to 1.19)
Absolute risk + BI-RADS density + BMI	0.60 (0.59 to 0.61)	1.22 (0.95 to 1.30)	0.61 (0.57 to 0.66)	1.09 (0.97 to 1.20)
Absolute risk + dense area + BMI	0.60 (0.59 to 0.61)	1.22 (0.95 to 1.30)	0.62 (0.59 to 0.62)	1.12 (0.94 to 1.23)
Absolute risk + percent density + BMI	0.60 (0.59 to 0.61)	1.19 (0.95 to 1.34)	0.63 (0.59 to 0.64)	1.13 (1.01 to 1.19)
BI-RADS + dense area + BMI	0.60 (0.59 to 0.61)	1.22 (0.95 to 1.30)	0.62 (0.59 to 0.62)	1.15 (0.89 to 1.20)
BI-RADS + percent density + BMI	0.60 (0.59 to 0.61)	1.24 (0.95 to 1.30)	0.62 (0.59 to 0.62)	1.12 (0.94 to 1.23)

[a] Each model also included age as a covariate. AUC = area under the curve; BCRAT = Breast Cancer Risk Assessment Tool; BI-RADS = Breast Imaging-Reporting and Data System; BMI = body mass index; O/E = observed to expected ratio.
[b] *P* values for comparisons of AUCs for risk models by race or ethnicity are not statistically significant.

(8). Future studies should evaluate whether volumetric breast density measures from digital breast tomosynthesis improve breast cancer risk prediction for Black and White women compared with 2D measures.

Data availability

Details of the study population and data collection are reported elsewhere (6) and will be made fully available at the time of publication.

Author contributions

Mattia Mahmoud, MPhil (Conceptualization; Formal analysis; Investigation; Methodology; Validation; Writing—original draft), Sarah Ehsan, MPH (Conceptualization; Data curation; Project administration; Writing—review & editing), Lauren Pantalone, MS (Data curation; Project administration; Writing—review & editing), Walter Mankowski, PhD (Data curation; Methodology; Software; Writing—review & editing), Emily F. Conant, MD (Investigation; Resources; Writing—review & editing), Despina Kontos, PhD (Investigation; Methodology; Resources; Software; Writing—review & editing), Jinbo Chen, PhD (Conceptualization; Investigation; Methodology; Writing—review & editing), Anne Marie McCarthy, PhD (Conceptualization; Funding acquisition; Investigation; Methodology; Validation; Writing—review & editing).

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Conflicts of interest

Emily Conant was on the grant and advisory panel of iCAD, Inc and was a speaker and on the advisory panel of Hologic, Inc. The remaining authors have no conflicts of interest to declare.

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