

Racial Differences in Mammographic Breast Density

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BACKGROUND. African American women have a lower incidence but a higher mortality from breast carcinoma than Caucasians. A proposed explanation for this discrepancy is the decreased efficacy of screening among African American women. Increased breast density in African American women may result in decreased sensitivity of mammography. The purpose of this article is to determine whether there is a difference in mammographic breast density between African American and Caucasian women.

METHODS. A series of 769 women were recruited from 5 sites. Mammograms were reviewed centrally by seven reviewers using Breast Imaging Reporting and Data System categories converted to numeric values. The mean mammographic densities for Caucasian, African American, and Latina patients were compared using a two-way analysis of covariance. The mean values for each race were estimated adjusting for the reader as well as for each patient's age and body mass index (BMI).

RESULTS. African American women had the lowest mean breast density. The reported density in this group was 2.43, compared with 2.69 among Caucasians and 2.65 among Latina patients. After adjusting for age and BMI as well as the reader, there was still an independent racial effect on breast density ($P = 0.0050$).

CONCLUSIONS. Mammographic breast density was lower in African American women than in Caucasians and Latinas. This discrepancy may be an intrinsic racial difference due to undetermined causes. Factors, such as the growth rate of tumors and the incidence of calcifications, must be studied to confirm that other forces do not have a negative impact on the efficacy of screening mammograms in African American women. *Cancer* 2003;98:590-6. © 2003 American Cancer Society.

KEYWORDS: mammography, breast density, African American women, body mass index, racial differences.

In the United States, breast carcinoma is more common among Caucasian women (annual incidence 115.5 per 100,000) than among African American women (annual incidence 101.5 per 100,000).¹ Although African American women have a lower incidence of breast carcinoma, they have a higher mortality (annual mortality 35.8 per 100,000) than Caucasians (annual mortality 27 per 100,000).¹ This mortality difference may be explained by the observation that African American women are more likely to have advanced-stage breast carcinoma at the time of diagnosis.^{2,3} Although the incidence of ductal carcinoma in situ in association with invasive breast carcinoma is comparable between African American and Caucasian women (18.6% vs. 16.4%, respectively),⁴ the incidence of Stage II disease at presentation is higher among African American women (31.6% vs. 27.8% respectively),⁴ as is the incidence of Stage III-IV disease (13.4% vs. 8.4%, respectively).⁴ This marked difference may be due to delays in diagnosis, which may be due to underutilization of screening mammography. Efforts are underway to increase utiliza-

tion.^{5,6} An alternative explanation is that there is decreased efficacy of screening among African American women.^{5,6}

It is reasonable to assume that if utilization of screening for cancer were comparable between African American and Caucasian women, the stage distribution of malignancies would be equivalent, unless differences exist in the efficacy of screening or in the inherent biology of the tumor. Efforts to increase utilization will not be sufficient to reverse disparities if efficacy is not equivalent.

One of the factors that can affect the efficacy of mammography is increased mammographic breast density, which will decrease the sensitivity of mammography.⁷⁻⁹ The purpose of this article is to determine whether there is a difference in mammographic breast density between African American and Caucasian women that might explain the difference in stage mix at presentation between these groups. To our knowledge, the association between breast density and race has not been explored previously.

MATERIALS AND METHODS

Between April 1997 and December 2000, 1293 patients were recruited at 5 participating sites into a study of computerized infrared imaging. The study was approved by the institutional review boards at each of the participating institutions and all patients provided informed consent before enrollment. Patients were eligible if they were undergoing a breast biopsy as a result of an abnormal mammogram and/or clinical findings. Patients were excluded from the study if they had undergone breast surgery within a year or if they had breast implants, breast reduction surgery, radiotherapy to the breast of interest, were pregnant, already had a histologically proven malignancy in the breast of interest, or weighed more than 136 kg (due to mechanical constraints). Of the initial cohort of patients, 1216 were recruited for the computerized infrared imaging study (Parisky YR, Sardi A, Hamm R, et al. Unpublished data, 2003).

Mammograms were available for 769 women. These images were reviewed centrally. Thirty women had bilateral films, due to the presence of suspicious lesions in both breasts.

Site personnel collected all patient demographic and study data on case report forms, which were verified by an independent clinical research organization (Quintiles MTC, Research Triangle Park, NC). The demographic data collected included age, race, height, and weight. Other recorded information included mammographic density interpretation by each reader, biopsy data, and lesion characteristics.

Mammograms were reviewed centrally by seven

reviewers who were blind to each other's findings. Breast density was categorized using Breast Imaging Reporting and Data System categories converted to numeric values as follows: 1, the breast is almost entirely fat; 2, the breast has scattered fibroglandular dense tissue; 3, the breast tissue is heterogeneously dense; 4, the breast tissue is extremely dense.¹⁰

From the 799 breasts of the 769 women with interpretable mammographic densities, 2112 interpretations were available. Not all of the reviewers read all of the mammograms. A mean of 2.8 readers independently interpreted the density of each breast. All of the mammographic densities were read centrally, regardless of their institution of origin. Mammograms were assigned randomly and distributed for interpretation among the different readers, regardless of the patient's demographics. Among the 7 readers there were 91-126 evaluations for the African American women and 222-323 evaluations for the Caucasian women.

Reviewers were not aware of either the other reviewers' reading or the final pathology results. Although readers also assessed the likelihood of cancer, this information is available elsewhere (Parisky YR, Sardi A, Hamm R, et al. Unpublished data, 2003). The only interpretation evaluated in the current study is the density measurement.

The mean mammographic densities for Caucasian, African American, and Latina patients were compared using a two-way analysis of covariance (ANCOVA). The mean values for each race were estimated and were adjusted for the reader as well as for the patient's age and body mass index (BMI). Pairwise *t* tests that compared the least squares means of density for the races were performed only if the overall test for the main effect of race was significant ($P \leq 0.05$).

The *P* values for this study were obtained using an ANCOVA despite the ordinal (nonparametric) nature of the four-point mammographic density scale. This was necessary to adjust for the differences among the readers as well as for any racial differences in the BMI (weight [kg] divided by height squared [m^2]) and age at the time of mammography. Furthermore, all analyses performed assumed the independence of the densities of the breasts in the 30 patients who had both breasts included in this study. They also assumed independence of the readers' assessment of the density of the same breast. As a result, the study implications are limited to the extent that these minor deviations from the theoretic requirements of ANCOVA caused inexact *P* values.

RESULTS

Although reviewers had different thresholds for reading the mammographic densities, the data reflect con-

TABLE 1
Mean Breast Density, Age, and Body Mass Index by Race

Race	No. of patients	No. of readings	Breast density (SD)	Age (SD; yrs)	BMI (SD; kg/m ²)
AA	207	586	2.43 (0.77)	55.6 (13.0)	31.3 (6.2)
Other	5	13	2.62 (0.51)	43.4 (8.4)	31.4 (4.2)
Latina	81	219	2.65 (0.79)	57.5 (12.5)	28.1 (5.7)
Caucasian	463	1262	2.69 (0.76)	55.8 (12.8)	27.4 (6.7)
Asian	13	32	3.09 (0.78)	49.2 (12.3)	23.2 (3.5)

SD: standard deviation; BMI: body mass index; AA: African American.

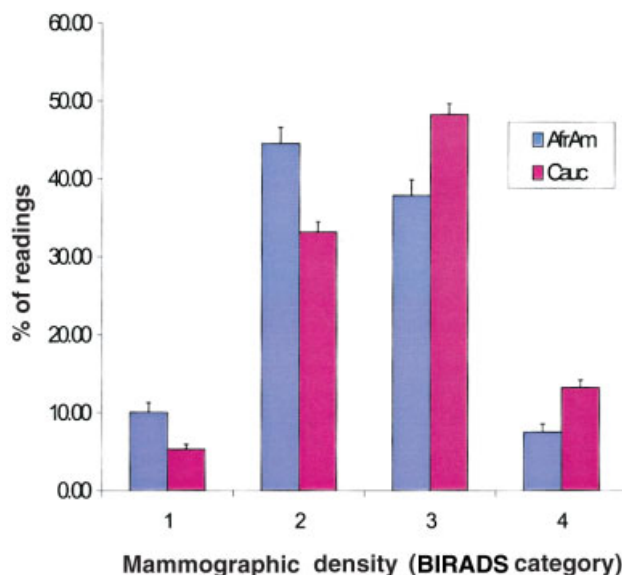
trol for this factor. For 80 of the 799 breasts examined, only 1 reader recorded a density. Of the remaining 719, there was complete agreement or a 1-point difference among readers for 703 breasts. There was a 44.6% complete agreement rate among all readers concerning the density of 321 breasts. However, of the 124 breasts interpreted by 2 different readers, there was agreement on 82 breasts (66.1%). Of the 595 breasts interpreted by 3 different readers, there was complete agreement on 239 breasts (40.2%). In only 16 cases, disagreement of more than 1 point was seen (either 1, 2, 3 [14 cases] or 2, 3, 4 [2 cases]).

African American women had the lowest mean breast density. The reported density in this group was 2.43, compared with 2.69 among Caucasians and 2.65 among Latina women. African American women also had a correspondingly higher mean BMI (31.3) than did the other 2 groups (Caucasians, 27.4; Latinas, 28.1; Table 1).

Figure 1 shows the distribution of mammographic density readings for African American and Caucasian women. There was a shift toward a lower density reading among African American women.

Some of the disagreement was attributed to different thresholds among readers. When the densities were adjusted for the reader, a significant racial effect remained ($P < 0.0001$). The adjusted mean densities were close to the raw means, indicating that the assignment of readers had not biased greatly the results by race. It is noteworthy that there was no statistically significant difference in mean mammographic densities (after adjusting for readers) between Latina and Caucasian patients ($P = 0.6065$).

Table 2 shows that there was still an independent racial effect ($P = 0.0050$) after adjusting for age, BMI, and reader. The estimated mean density for African American women would increase from 2.43 to 2.54 if they were the same age and had the same BMI as the other races. Despite this change, their mean density would still be significantly lower than that of Latina, Caucasian, and Asian women. Figure 2 shows the ob-

**FIGURE 1.** Distribution of mammographic density readings (using Breast Imaging Reporting and Data System [BIRADS] categories) for African American and Caucasian women. A significant shift toward lower density readings is noted for African American women. AfrAm: African American; Cauc: Caucasian.

served difference in both the mean and the adjusted mean breast density between African American and Caucasian women. The estimated mean density for Asian women would decrease from 3.09 to 2.79 if they were the same age and BMI as the other races. Their mean density no longer would be significantly different from the other races (except, of course, African American women).

DISCUSSION

Racial differences in the breast carcinoma survival rate exist between African American and Caucasian women. For example, the 5-year survival rate among African American women is 62% compared with 78% for Caucasian women.¹¹ Mortality is also higher among African American women.¹ Although mortality

TABLE 2
Modeled Density by Race, Adjusted for Evaluator, Age, and Body Mass Index^a

Race	Adjusted mean density (P) ^b	African American (P) ^b	Latina (P) ^b	Caucasian (P) ^b
African American	2.54			
Other	2.55	0.9479		
Latina	2.67	0.0139		
Caucasian	2.66	0.0006	0.7969	
Asian	2.79	0.0372	0.3294	0.2558

^aAlthough the adjusted mean densities are substantially different, African-American women still demonstrate a significantly lower breast density compared with other racial groups and after adjusting for evaluator, age, and body mass index.

^bBreast Imaging Reporting and Data Systems (BIRADS) categories were used for density readings.

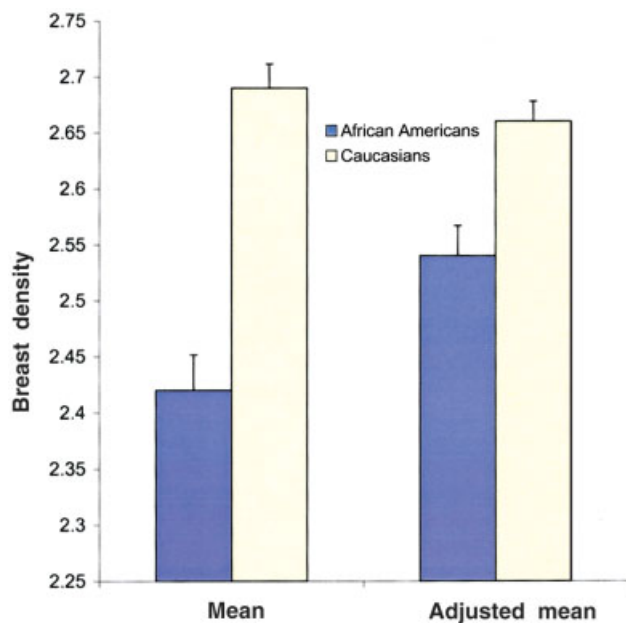


FIGURE 2. After adjusting for evaluator, age, and body mass index, African American women had a higher mean breast density. The adjusted mean density is still significantly lower than the adjusted mean density for Caucasian women ($P = 0.0006$).

has decreased among Caucasian women during the past decade, this trend has not occurred for African American women. This difference may be due to the more advanced-stage disease at presentation among African American women.^{2,3}

Decreased availability and/or utilization of screening mammography by African American women has been implicated as the major cause of this difference in stage at presentation.^{2,3,6,12-15} For this reason, major efforts have been undertaken to increase the availability and utilization of mammography by African American women.^{3,14,15}

Another confounding factor for the higher stage at presentation may be decreased intrinsic efficacy of screening mammography among African American women. If mammography were equally effective for African-American and Caucasian women, then complete adherence to the guidelines of the American Cancer Society (ACS) in both populations would reverse the disparity. However, it is not clear that this is the case and it is possible that universal adherence to ACS guidelines may be insufficient.

One of the factors that may affect the efficacy of mammography is breast density. Mammography is less sensitive in patients with increased breast density, making an early malignant process more difficult to detect.⁷⁻⁹ Therefore, the sensitivity of screening mammography should be inversely proportional to the mammographic density of the group screened. Racial differences in breast density have not been explored adequately until now.

Univariate analysis demonstrated that mammographic breast density is actually lower in African American women compared with Caucasian women. The mean breast density of 2.43 among African American patients was significantly lower than the Caucasian mean breast density of 2.69 and the Latina mean breast density of 2.65. A racial difference was not found when the breast density readings of Latina and Caucasian patients were compared. This would suggest that screening mammography should be equally or more effective among African American women, if all other factors are equal.

Mammographic density is inversely proportional to weight and/or BMI.^{16,17} In their study, White et al.¹⁶ reported that BMI had a strong association with breast density. For example 53% of women in the lowest BMI quartile had an extremely dense breast compared with only 5% of women in the upper BMI quartile. In our study, African American women had a higher average weight and BMI than Caucasian and Latina women. The National Institutes of Health (NIH) identify overweight as a BMI of 25–29.9 kg/m² and obesity as a BMI of 30 kg/m² or greater.¹⁸ The combined incidence of overweight and obesity (BMI \geq 25 kg/m²) in women age 20 and older is 65.8% for African American women, 65.9% for Mexican-American women, and 49.2% for Caucasian women.¹⁸ In our population of women, the combined incidence of overweight and obesity (BMI \geq 25 kg/m²) was 79% for African American women, 57% for Caucasians, and 69% for Latinas. The difference in our study could have been influenced by the age difference. Specifically, the patients in our study had a mean age of 55 years, which represents an older cohort than the general population identified by the NIH. A similar difference in the age of

the African American and Caucasian patients in the current study and the general population was noted.

Breast density decreases with age.^{16,19} One series confirmed the lower sensitivity and specificity of mammography in younger women.¹⁹ Younger patients, when compared with older women, were more likely to have large, nonpalpable tumors, which were associated with higher mammary density.¹⁹

In our study, density was recalculated in a multivariate analysis, adjusting for evaluator, age, and BMI. Although attenuated, the racial difference in breast density still persisted. The adjusted mean breast density of 2.54 among African American patients was still significantly lower than the Caucasian mean breast density of 2.66 and the Latina mean breast density of 2.67. Agreement on the classification of mammographic patterns among different readers has been consistent and reproducible.^{20,21} In the study by Carlile et al.,²⁰ 12 radiologists classified mammography readings with minimal interobserver variation. In the current study, seven radiologists interpreted the mammograms and their readings were also consistent and reproducible.

The mean breast density among African American patients still would be significantly lower than that of Caucasian, Latina, and Asian patients, even if they were the same age and had the same BMI. Possible causes of this difference in breast density would include nutrition, lifestyle, genetic and familial inheritance, parity, and hormonal status.²²⁻²⁸ A genetic component has been shown to influence mammographic breast density,²⁹ which may explain the racial differences documented in our study.

If breast density were the only determinant of the efficacy of screening mammography, our study would suggest that mammography was more effective for African American women, because their breast density is lower relative to Caucasian and Latina women. However, numerous other factors affect the efficacy of screening mammography, such as the age of presentation and tumor growth rate.

Differences in age may significantly impact the efficacy of screening. Among Caucasian women, 6.7% of breast carcinomas are diagnosed in women younger than the age of 40, whereas about 16.4% of African American women with breast carcinoma are younger than age 40 years.³⁰ Therefore, yearly mammography beginning at age 40 will miss at least 6.7% and at least 16.4% of breast carcinomas among Caucasian and African American women, respectively. Complete adherence to the ACS guidelines of yearly mammography beginning at age 40 will, at most, identify 93.3% and 83.6% of breast carcinomas among Caucasian and African American women, respectively.

Tumor growth rate also has significant implications for the efficacy of screening. The yearly interval for screening mammography is based on the doubling time of breast tumors. There is a window of opportunity between the time a tumor becomes visible on mammography and the time it will become clinically palpable (sojourn time). The faster the doubling time, the shorter this window of opportunity. Biologic differences among African American women cause tumors to behave more aggressively compared with other racial groups. Tumors in African American women have been characterized by a younger age of diagnosis, larger size, and less favorable histology,^{2,5,30,31} such as higher degree of necrosis, lymph node-vascular space involvement, perineural invasion, and less frequency of hormone receptor positivity (both estrogen and progesterone receptors).³²⁻³⁷ All of these factors suggest that African American women have biologically more aggressive tumors, and thus are likely to have shorter doubling times. If this is true, the 1-year interval between mammograms may be less effective.

Although bra size was not recorded in this study, it is reasonable to assume that as the African American women in this study and nationally have a higher average BMI, they may be larger breasted too, which might affect mammographic quality (e.g., longer radiographic exposure and increased motion artifact). There are other implications for women with larger breasts, in terms of both clinical and self-breast examinations. Detection by physical examination of small lesions in the larger breast can be more challenging. In contrast, both clinical and self-breast examinations may be even more adequate screening tools for small tumors in women with less dense and smaller breasts.

Some investigators have suggested that breast density may be a risk predictor for breast carcinoma. However, most studies of breast carcinoma risk have failed to incorporate this measurement.^{22,29,38-40} The role of mammographic breast density as a risk factor remains controversial and was not the focus of interest in the current investigation. Future studies of racial differences may be able to elucidate other factors that predict breast density, the impact of density measures, and how changes in mammographic density over time can affect breast carcinoma risk.

In our study, racial differences remain an important factor in the documented breast density disparity, even after accounting for differences in BMI and age. The implications of this observation are of paramount importance when contemplating possible interventions that may result in altering the documented worse prognosis from breast carcinoma among this subset of the population. Specifically, mammography can be considered to be an effective screening tool among African American women. Given the noted re-

duction in breast density, malignant lesions should be easier to detect and diagnose mammographically in these patients. Our observation that the differences in density persist even after correcting for age invite the proposition that the less dense breast tissue in this younger subset of the population would be amenable to mammographic screening. If racial disparities are to be reconciled, consideration should be given to recruiting younger African American women to mammographic screening programs.

Although our study finds a conclusive relationship between mammographic breast density and race, many other factors contributing to the racial disparity that exists in breast carcinoma are unclear and need further exploration. Mammographic breast density was lower in African American women than in Caucasian and Latina women. This difference can be somewhat explained by differences in BMI, but is also intrinsically a racial difference due to undetermined causes. As breast density is the same or lower than in Caucasian and Latina women, the efficacy of mammography among African American women based on this factor should be equivalent or better. Other factors, such as the growth rate of tumors and the incidence of calcifications must be studied to confirm that other forces do not have a negative impact on the efficacy of screening mammograms among African American women.

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