Title

Mammographic densities of Aboriginal and non-Aboriginal women living in Australia's Northern Territory

Authors

Kriscia A Tapia[1], Gail Garvey[1,2], Mark F McEntee[4], Mary Rickard[1,5], Lorraine Lydiard[3], Patrick C Brennan[1]

1 Faculty of Health Sciences, The University of Sydney, New South Wales, Australia

2 Charles Darwin University, Wellbeing and Preventable Chronic Diseases Division Menzies School of Health Research, Casuarina, NT Australia

3 BreastScreen Northern Territory, Australia

4 Department of Medicine, University College Cork, Ireland

5 BreastScreen New South Wales, Sydney, NSW, Australia

Abstract

OBJECTIVES: To compare the mammographic densities and other characteristics of Aboriginal and non-Aboriginal women screened in Australia. METHODS: Population screening programme data of Aboriginal (n = 857) and non-Aboriginal women (n = 3236) were used. Mann-Whitney U test compared ages at screening and Chi-square tests compared personal and clinical information. Logistic regression analysis was used for density groupings. OR and 95% CI were calculated for multivariate association for density. RESULTS: Mammographic density was lower amongst Aboriginal women ($P < 0.001$). For non-Aboriginal women, higher density was associated with younger age (OR 2.4, 95% CI 2.1-2.8), recall to assessment (OR 2.2, 95% CI 1.6-3.0), family history of breast cancer (OR 1.4, 95% CI 1.2-1.6), English-speaking background (OR 1.4, 95% CI 1.2-1.6), and residence in remote areas (OR 1.2, 95% CI 1.1-1.4). For Aboriginal women, density was associated with younger age (OR 2.7, 95% CI 2.0-3.5; $P < 0.001$), and recall to assessment (OR 2.3, 95% CI 1.4-3.9; $P < 0.05$). CONCLUSIONS: Significant differences between Aboriginal and non-Aboriginal women were found. There were more significant associations for dense breasts for non-Aboriginal women than for Aboriginal women.

Keywords

Aboriginal Australians; Mammographic density; Breast cancer

Introduction

Female breast cancer accounts for 25% of all cancers diagnosed in Aboriginal and Torres Strait Islander Australians, henceforth respectfully referred to as Aboriginal, with an estimated 1 in 11 Aboriginal women developing the disease [1, 2]. Although breast cancer incidence is lower by up to 20% for Aboriginal women compared with other Australians, Aboriginal women experience poorer prognoses with consistently lower survival rates and higher rates of death [3, 4]. The inequalities in outcomes are well documented and have been attributed to a combination of factors and disparities between Aboriginal and non-Aboriginal people. Evidence suggest that Aboriginal women are more likely than their non-Aboriginal counterparts to experience socio-economic disadvantage, present with co-morbidities, live in more remote locations, are younger at diagnosis with more distant spread or advanced breast cancer, and are less likely to participate in breast screening [2, 4-8]. However, studies on risk factors for breast cancer specifically relevant to Aboriginal Australians are currently scarce, thus limiting cancer control strategies for this group of women in Australia.

Breast density refers to the composition of fibroglandular and fat tissues in the breast and is well reported as having a strong direct relationship with breast cancer risk. Women with predominantly fatty or low dense breasts, regardless of the presence of other risk factors such as age, menopausal status, genetics, hormonal agents, and elements of lifestyle, confer a lower risk for breast cancer [9]. Moreover, breast density is also reported to affect mammographic sensitivity with evidence of highly dense breasts presenting challenges for radiologists in detecting invasive cancers [10]. Mammographic density can be measured by both qualitative and quantitative methods, via automated tools and manual means using area and volume percentages or specific classification techniques [11]. The Australian BreastScreen programme and the Royal Australian and New Zealand College of Radiologists have provided guidelines for the reporting of density in clinical practice using four categories similar to the American College of Radiology, Breast Imaging Reporting and Data System (BI-RADS) version 4 (2003) lexicon [12]. While Australian clinicians are encouraged by governing bodies to include density grades in clinical reports, there is currently no mandate to routinely provide women with information about breast density, nor routinely recommend supplemental imaging procedures for women with dense breasts. In the USA, at the time of writing this article, 32 states have passed legislation for women who have undergone mammography to be notified of breast density and their risks.

Ethnic variations in breast density and associations with breast cancer risks have been shown in different populations around the world although reasons for variations remain unclear. Aleut and Native American women of Alaska reported lower mammographic density than Eskimo women [13], and African-American women had lower median per cent density compared with Asian-Americans [14]. Caucasian women in the UK had higher age-adjusted mean per cent density than South Asian, and Afro-Caribbean women [15]. In New Zealand, Caucasian women were found to have lower volumetric density than Maori women but not lower than Pacific Islander women, and Asians had the highest measures amongst all women [16]. Evidence for the variation between the breast density measures of Aboriginal and non-Aboriginal Australians is yet to be demonstrated. The aim of the current work is to profile the mammographic densities of Aboriginal and non-Aboriginal women in the NT where up to 30% of the population identifies as Aboriginal. Differences in the demographical and personal characteristics of Aboriginal and non-Aboriginal women will also be investigated and density covariates within populations of women will be explored.

Methods

Ethical approval was provided by the Human Research Ethics Committee (HREC) of the NT Department of Health and Menzies School of Health Research (HREC 2016-2627). The Aboriginal Health and Medical Research Council of New South Wales were informed of this study as the statistical analysis of data pertaining to Aboriginal Australians was conducted in New South Wales (NSW). Written consent to use information collected during breast screening was obtained from each participant at the time that they were screened.

The study was performed retrospectively using a client data sample retrieved from BreastScreen NT, a population screening programme. The sample consisted of 4093 (857 self-reported as Aboriginal and 3236 as non-Aboriginal) women aged between 40 and 85 years who were routinely screened between 30 March and 24 November 2015. Breast mammograms were performed at permanent screening facilities in Darwin, Palmerston, and Alice Springs, and via the BreastScreen NT mobile bus units that service remote to very remote communities in the NT. Digital image files were sent electronically to Sydney Breast Clinic (SBC) in NSW, for radiologist interpretation. Each case was read by two radiologists who allocated a ‘Recall’ or ‘Normal’ finding and where two radiologists gave conflicting decisions (n = 302), a third radiologist acted as arbitrator.

Radiologists at SBC used the American College of Radiology BI-RADS version 4 (2003) to allocate each case with a mammographic density score from 1 to 4. The density categories are defined as: 1 = almost entirely fatty, approximately 0–25% density; 2 = scattered areas of fibroglandular density, approximately 25–50% density; 3 = heterogeneously dense, approximately 50–75% density; and 4 = extremely dense, approximately 75–100% density. Density scores were given by either one or two radiologists at SBC at the time of screen reading. In instances where two radiologists’ density scores varied by more than 1 BI-RADS score (n = 24), a third reader was asked to arbitrate. In all other cases with density scores disagreement of only 1 BI-RADS score (n = 970), the middle score was used [17]. Women with breast implants (n = 46) were excluded from this study.

Women's personal details such as date of birth, residential and postal address, Aboriginal status, English speaking background (ESB) or non-English-speaking background (NESB), family history of breast cancer, previous breast cancer and year of diagnosis, current symptoms, and use of hormone replacement therapy (HRT) within the last 6 months, were extracted from the NT Department of Health computerised database. This information was obtained from the Personal Information and Consent forms that are routinely completed by clients prior to screening. Personal information was linked to clinical notes before the investigators of this study de-identified the data for analysis.

Women's residential addresses were categorised based on the Australian Statistical Geographical Standards Remoteness Areas classification (ASGSRA) [18]. In the NT, only three categories are available: outer regional, remote, and very remote. The capital city, Darwin, is classed as outer regional because it is not considered to be a provider of Category A services in education and health, nor does it have a population equal to or more than 250,000 persons.

In the first stage of analysis, baseline differences between Aboriginal and non-Aboriginal women were explored. Due to the non-Gaussian nature of the data, the median age of women screening was analysed by Mann–Whitney U test. Categorical variables such as density groupings, HRT use, family history of breast cancer, current symptoms, previous breast cancer diagnosis, geographical remoteness, language background, and case outcome were analysed using Chi-square test.

The second part of the analysis treated density as a dichotomous variable and compared women with dense breasts (BI-RADS 3 and 4) with those having fatty breast (BI-RADS 1 and 2) for all screened women, Aboriginal women only, and finally non-Aboriginal women only. The difference for age, a non-normally distributed continuous variable, was analysed using a Mann–Whitney U test, and categorical variables (geographical remoteness, language background, HRT use, family history of breast cancer, previous breast cancer diagnosis, symptoms and case outcome), were analysed using Chi-square tests. ROC curve analysis was used to determine a cut-off point which best facilitated allocation of these variables into two groups: above and below cut-off points [19]. For example, the cut-off point for age which best separated women based on density was 55 years. Using this cut-off value, unconditional logistic regression was used to derive OR and 95% CIs. A P value was obtained from a two-tailed test, and a P value of\0.05 was considered significant. Multivariate logistic regression was performed on variables with univariate association of P B 0.2. Variables were retained in the model if $p<0.1$ to determine OR and 95% CI. The IBM SPSS version 24 statistical software was employed for the analysis.

Results

Women's characteristics

Several significant differences were seen between the characteristic of Aboriginal and non-Aboriginal women, and these are summarised in Table 1. Aboriginal women were significantly younger than non-Aboriginal women ($p<0.001$) with median ages of 54 years (IQR 48–60 years) and 57 years (IQR 52–63 years), respectively. A lower proportion of Aboriginal women were living in outer regional areas compared with non-Aboriginal women with more Aboriginal women living in remote to very remote locations ($p<0.001$). English was the predominant language spoken by non-Aboriginal women and for Aboriginal women a larger proportion spoke Aboriginal languages ($p<0.001$). Mammographic density was lower amongst Aboriginal compared with non-Aboriginal women, while Aboriginal women were less likely to use HRT compared with non-Aboriginal women ($p<0.001$). Finally, Aboriginal women reported less family history of breast cancer compared with their non-Aboriginal counterparts. No other significant differences were shown for the characteristics, and full details are given in Table 1.

Table 1. Characteristics of women by Aboriginal and non-Aboriginal statuses

Variables		Aboriginal N (%)	Non-Aboriginal N (%)	p value
Age (y)				
	Median (Q1, Q3)	54 (48,60)	57 (52,63)	<0.001[a]
	<55	481 (56.1%)	1399 (43.2%)	<0.001[b]
	≥55	376 (43.9%)	1837 (56.8%)	
Place of residence [c]				
	Outer regional	118 (13.8%)	1823 (56.9%)	<0.001[b]
	Remote	579 (67.7%)	1172 (36.2%)	
	Very remote	159 (18.6%)	209 (6.5%)	
English speaking background (ESB)				
	ESB	245 (28.7%)	2721 (84.2%)	<0.001[b]
	Non-ESB	610 (71.3%)	511 (15.8%)	
	non-English language type			
	Aboriginal language	607 (99.5%)	7 (1.4%)	<0.001[b]
	Other language	3 (0.5%)	504 (98.6%)	
Mammographic density (BI-RADS)				
	1	169 (19.7%)	424 (13.1%)	<0.001[b]
	2	353 (41.2%)	1207 (37.3%)	
	3	240 (28%)	963 (29.8%)	
	4	95 (11.1%)	642 (19.8%)	
	Fatty breast (1,2)	522 (60.9%)	1631 (50.4%)	<0.001[b]
	Dense breast (3,4)	335 (39.1%)	1605 (49.6%)	
HRT use within 6 months [e]				
	No	840 (98%)	2950 (91.4%)	<0.001[b]
	Yes	17 (2%)	278 (8.6%)	
Family history of breast cancer [f]				
	No	613 (80.7%)	1961 (66.1%)	<0.001[b]
	Yes	147 (19.3%)	1007 (33.9%)	
	1st degree relative [g]	61 (75.3%)	429 (67%)	0.13[b]
	2nd degree relative [g]	20 (24.7%)	211 (33%)	
Previous breast cancer diagnosis				
	No	485 (98.6%)	3161 (97.7%)	0.09[b]
	Yes	12 (1.4%)	75 (2.3%)	
Current lump				
	No	828 (96.6%)	3121 (96.4%)	0.81[b]
	Yes	29 (3.4%)	115 (3.6%)	
Current nipple discharge				
	No	851 (99.3%)	3215 (99.4%)	0.86[b]
	Yes	6 (0.7%)	21 (0.6%)	
Case decision				
	Normal	729 (92.4%)	3039 (93.9%)	0.11[b]
	Recalled	65 (7.6%)	197 (6.1%)	

[a] Reported by a Mann-Whitney U test; [b] Reported by a Pearson Chi-square test; [c] Visitors (n=33) were excluded; [d] Not known (n=6) was excluded; [e] Not known (n=1) was excluded; [f] Not known (n=365) were excluded; [g] Not known (n=390) and paternal (n=43) were excluded

Mammographic density in all women grouped together

Univariate analysis was used to examine factors associated with density for all women, and the data are summarised in Table 2. Odds ratios were calculated to quantify the associations of variables to high density. A significant difference was evident between the mean ages of women with dense breasts (BI-RADS 3 and 4) versus fatty breasts (BI-RADS 1 and 2), at 54.8 and 58.2 years, respectively ($p<0.001$). The ROC analysis determined an age cut-off of 55 years which best separated women based on density. Women below this threshold were 2.3 times more likely to have dense breasts compared with women above the cut-off (95% CI 2.0–2.6; $p<0.001$). Other significant associations with density that were observed were: non-Aboriginal women were 50% more likely to have dense breasts than Aboriginal women (OR 1.5, 95% CI 1.3–1.8; $p<0.001$); individuals with a non-English-speaking background (NESB) that were not Aboriginal-language speakers were 70% more likely to have dense breasts than Aboriginal-language speakers (OR 1.7, 95% CI 1.3–2.1; $p<0.001$); participants with family histories of breast cancer were 40% more likely to have dense breasts compared with women who reported no family history of breast cancer (OR 1.4, 95% CI 1.2–1.6; $p<0.001$); individuals who reported having a breast lump were 50% more likely to have dense breasts compared with those who did not (OR 1.5, 95% CI 1.1–2.2; $p<0.05$); and recalled women were 2.2 times more likely to have dense breasts than non-recalled cases (95% CI 1.7–2.8; $p<0.001$). No other significant differences were observed. The association of HRT use and density resulted in $p=0.05$ (OR 1.3, 95% CI 1.0–1.6; P 0.05), and this was retained in the model and tested for multivariate association in the next stage of analysis.

Table 2 Association of density with other characteristics for all women

Variables	Fatty Breast N (%)	Dense Breast N (%)	p value	OR (95% CI)
Age (y)				
Median (Q1, Q3)	54 (48,60)	57 (52,63)	<0.001[a]	
≥55	1451 (61.3%)	915 (38.7%)	<0.001[b]	2.3 (2.0-2.6)
<55	702 (40.6%)	1025 (59.4%)		
Aboriginal status				
Aboriginal	522 (60.9%)	335 (39.1%)	<0.001[b]	1.5 (1.3-1.8)
Non-Aboriginal	1631 (50.4%)	1605 (49.6%)		
Place of residence				
Outer regional	1040 (53.3%)	912 (46.7%)	0.44[b]	1.0 (0.9-1.2)
Remote and very remote	1104 (52.1%)	1016 (47.9%)		
English speaking background (ESB)				
Non-ESB	604 (53.9%)	517 (46.1%)	0.31[b]	1.1 (0.9-1.2)
ESB	1545 (52.1%)	1421 (47.9%)		
non-English language type				
Aboriginal language	367 (59.8%)	247 (40.2%)	<0.001[b]	1.7 (1.3-2.1)
Other language	237 (46.7%)	270 (53.3%)		
HRT use within 6 months				
No	2014 (53%)	1783 (47%)	0.05[b]	1.3 (1.0-1.6)
Yes	139 (47.1%)	156 (52.9%)		
Family history of breast cancer				
No	1412 (54.9%)	1162 (45.1%)	<0.001[b]	1.4 (1.2-1.6)
Yes	544 (47.2%)	610 (52.9%)		
1st degree relative [c]	228 (46.5%)	262 (53.5%)	0.36[b]	1.2 (0.9-1.6)
2nd degree relative [c]	99 (42.9%)	132 (57.1%)		
Previous breast cancer diagnosis				
Yes	50 (57.5%)	37 (42.5%)	0.36[b]	1.2 (0.8-1.9)
No	2103 (52.8%)	1903 (47.2%)		
Current lump				
No	2092 (53%)	1857 (47%)	<0.05[b]	1.5 (1.1-2.2)
Yes	61 (42.4%)	83 (57.6%)		
Current nipple discharge				
No	2141 (52.7%)	1925 (47.3%)	0.39[b]	1.4 (0.6-3.0)
Yes	12 (44.4%)	15 (55.6%)		
Case decision				
Normal	2062 (53.8%)	1769 (46.2%)	<0.001[b]	2.2 (1.7-2.8)
Recalled	91 (34.7%)	171 (65.3%)		

[a] Reported by Mann-Whitney U test; [b] Reported by a Pearson Chi-square test; [c] Not known (n=390) and paternal (n=43) were excluded. Note: The reference groups for ORs are always presented in the first row of the variables.

Using the significant variables in Table 2, multivariate stepwise logistic regression analysis demonstrated that the significant predictors for dense breasts for all women were family history of breast cancer (OR 1.3, 95% CI 1.1–1.5; p<0.001), non-Aboriginal status (OR 1.7, 95% CI 1.4–2.0; p<0.001), recalled case (OR 2.3, 95% CI 1.7–3.0; p<0.001), and being under 55 years of age (OR 2.5, 95% CI 2.1–2.8; p<0.001) (Figure 1).

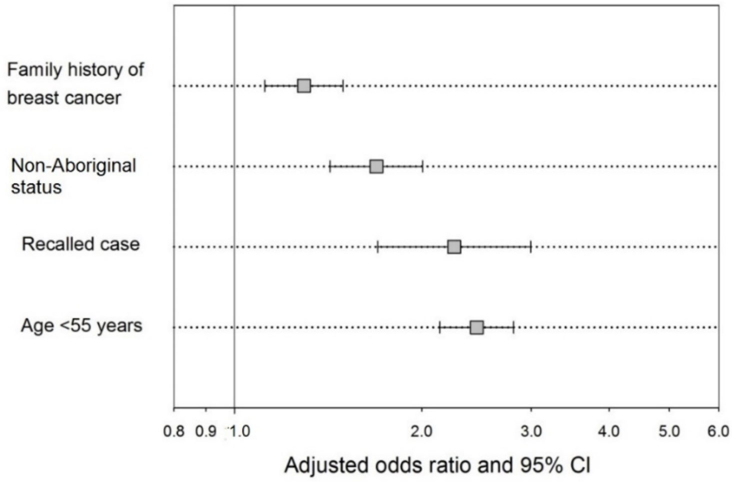

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Figure 1. Factors associated with high mammographic density (BI-RADS 3 and 4) for all women screened in the NT in 2015.

Mammographic density of women allocated to Aboriginal or non-Aboriginal groups

The second part of this study evaluated factors associated with density within Aboriginal women and non-Aboriginal women separately. Full details are shown in Table 3. Amongst Aboriginal women, the characteristics that are significantly associated with density were age, with women younger than 55 years 2.7 times more likely to have dense breasts than older women (95% CI 2.0–3.5; p<0.001), and case decision, with recalled women 2.3 times more likely to have dense breasts compared with women whose cases were considered normal (95% CI 1.4–3.9; p<0.05). For non-Aboriginal women, the characteristics that are significantly associated with density are younger age (OR 2.4, 95% CI 2.1–2.8; p<0.001), residence in remote locations (OR 1.2, 95% CI 1.1–1.4; p<0.05), English speaking background (ESB) (OR 1.4, 95% CI 1.2–2.6; p<0.05); family history of breast cancer (OR 1.4, 95% CI 1.2–1.6; p<0.001), current lump (OR 1.5, 95% CI 1.0–2.2; p<0.05), and recalled case (OR 2.2, 95% CI 1.6–3.0; p<0.001).

Table 3. Association of density with characteristics of Aboriginal women and non-Aboriginal women

	Aboriginal				Non-Aboriginal			
Variables	**Fatty Breast N (%)**	**Dense Breast N (%)**	**p value[a]**	**OR (95% CI)**	**Fatty Breast N (%)**	**Dense Breast N (%)**	**p value[a]**	**OR (95% CI)**
Age (y)								
≥ 55	291 (72.9%)	108 (27.1%)		1.0 (Ref)	1160 (59%)	807 (41%)		1.0 (Ref)
< 55	231 (50.4%)	227 (49.6%)	<0.001	2.7 (2.0-3.5)	471 (37.1%)	798 (62.9%)	<0.001	2.4 (2.1-2.8)
Place of residence								
Outer regional	77 (64.7%)	42 (35.3%)			963 (52.5%)	870 (47.5%)		
Remote to very remote	445 (60.3%)	293 (39.7%)	0.36	1.2 (0.8-1.9)	659 (47.7%)	723 (52.3%)	<0.05	1.2 (1.1-1.4)
English speaking background (ESB)								
ESB	154 (62.9%)	91 (37.1%)			236 (46.2%)	275 (53.8%)		
Non-ESB	368 (60.3%)	242 (39.7%)	0.49	1.1 (0.8-1.5)	1391 (51.1%)	1330 (48.9%)	<0.05	1.4 (1.2-1.6)
non-English language type								
Other language	2 (66.7%)	1 (33.3%)			235 (46.6%)	269 (53.4%)		
Aboriginal language	366 (60.3%)	241 (39.7%)	0.82	1.3 (0.1-14.7)	1 (14.3%)	6 (85.7%)	0.09	5.2 (0.6-43.5)
HRT use within 6 months								
No	511 (60.8%)	329 (39.2%)			1503 (50.8%)	1454 (49.2%)		
Yes	11 (64.7%)	6 (35.3%)	0.75	0.9 (0.3-2.3)	128 (46%)	150 (54%)	0.13	1.2 (1.0-1.6)
Family history of breast cancer								
No	369 (60.2%)	244 (39.8%)			1043 (53.2%)	918 (46.8%)		
Yes	87 (59.2%)	60 (40.8%)	0.82	1.0 (0.7-1.5)	457 (45.4%)	550 (54.6%)	<0.001	1.4 (1.2-1.6)
1st degree relative	37 (60.7%)	24 (39.3%)			191 (44.5%)	238 (55.5%)		
2nd degree relative	10 (50%)	10 (50%)	0.40	1.5 (0.6-4.3)	89 (42.2%)	122 (57.8%)	0.57	1.1 (0.8-1.5)
Previous breast cancer diagnosis								

	Yes	8 (66.7%)	4 (33.3%)			1589 (53.3%)	1572 (49.7%)		
	No	514 (60.8%)	331 (39.2%)	0.68	1.3 (0.4-4.3)	42 (56%)	33 (44%)	0.33	1.3 (0.8-2.0)
Current lump									
	No	508 (61.4%)	320 (38.6%)			1584 (50.8%)	1587 (49.2%)		
	Yes	14 (48.3%)	15 (51.7%)	0.16	1.7 (0.8-3.6)	47 (40.9%)	68 (59.1%)	<0.05	1.5 (1.0-2.2)
Current nipple discharge									
	No	519 (61%)	332 (39%)			1622 (50.5%)	1593 (49.5%)		
	Yes	3 (50%)	3 (50%)	0.58	1.6 (0.3-7.8)	9 (42.9%)	12 (57.1%)	0.49	1.4 (0.6-3.2)
Case decision									
	Normal	495 (62.5%)	297 (37.5%)			1567 (51.6%)	1472 (48.4%)		
	Recalled	27 (41.5%)	38 (58.5%)	<0.01	2.3 (1.4-3.9)	64 (32.5%)	133 (67.5%)	<0.001	2.2 (1.6-3.0)

[a] *Reported by a Pearson Chi-square test. Note: The reference groups for ORs are always presented in the first row of each variable*

Using the significant variables in Table 3, multivariate stepwise logistic regression analysis demonstrated the characteristics most strongly associated with density in groups of women separately (Figure 2). For Aboriginal women, density was associated with younger age (OR 2.7, 95% CI 2.0–3.5) and case decision (OR 2.3, 95% CI 1.4–3.9). For non-Aboriginal women, density was associated with younger age (OR 2.4, 95% CI 2.1–2.8), recalled case (OR 2.2, 95% CI 1.6–3.0), family history of breast cancer (OR 1.4, 95% CI 1.2–1.6), English-speaking background (ESB) (OR 1.4, 95% CI 1.2–1.6), and residence in remote areas (OR 1.2, 95% CI 1.1–1.4).

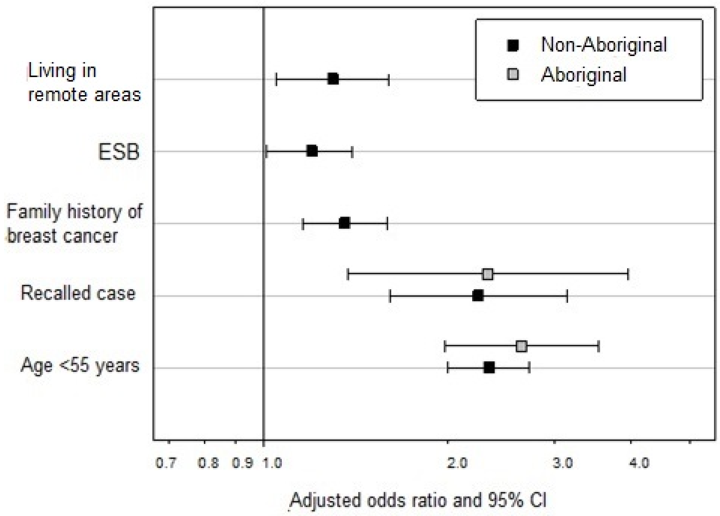

Figure 2.Factors associated with high mammographic density (BI-RADS 3 and 4) for Aboriginal and non-Aboriginal women screened in the NT of Australia in 2015.

Key: ESB refers to English-speaking background

Discussion

These findings describe the characteristics of the breast screening population in the NT of Australia. Prior to this study, evidence of variations between the BI-RADS mammographic densities of Aboriginal and non-Aboriginal women from an Australian screening population was unavailable. The current work highlights the differences between Aboriginal and non-Aboriginal women and identifies the factors strongly associated with mammographic density. Consistent with national population statistics and evidence from previous studies in the screening population [4, 20, 21], this study found that Aboriginal women were younger at screening than their non- Aboriginal counterparts with 12.9% fewer Aboriginal women over 55 years. Even so, average mammographic density was significantly lower amongst Aboriginal women compared with non-Aboriginal women. This finding is congruent with a previous study that used the Tabar method to classify mammographic parenchymal pattern and showed that

Aboriginal women in a NSW screening programme had predominantly fatty breasts [22]. Our study, however, is the first, to our knowledge, to report density profiles of Aboriginal Australians using the widely employed BI-RADS version 4 (2003) approach.

Younger age was the strongest covariate for mammographic density for both Aboriginal and non-Aboriginal women. This finding is aligned with the well-established inverse relationship between age and density [23]. Internationally, evidence in USA [13, 14], UK [15], Asia [24, 25], and New Zealand [16] report variations in densities between ethnic groups and the reasons for these differences remain unclear. A recent study that examined breast density across 40 ethnicities and location-specific populations in 22 countries found that common to all women and regardless of ethnicity, the menopausal status of any age had the strongest association with breast density [26]. While this current work is limited by the absence of women's menopausal statuses, other variables were found to be strongly associated with density.

Cases that were recalled for further tests were more likely to be mammographically dense than those that were not, and this was strongly associated with density for all women. One explanation is that dense breasts are more complex to interpret, and it is more difficult to be confident that the appearances are normal, hence yielding higher recall rates. Another explanation could be the well-established positive association between mammographic density and breast cancer risk that radiologists are likely attuned to. This awareness of risk was demonstrated by the study by Al Mousa and colleagues that used eye-tracking analysis and found that the performance of expert radiologists improved for cases with increased mammographic density [27, 28]. It demonstrated that density presents an important visual cue signifying higher risk. While our findings cannot comment on cancer detection rates in the absence of pathology data, the tendency to recall dense breasts in this sample underscores the radiologists' perceived increased breast cancer risk in these cases.

Previous studies have shown that women with higher breast density were more likely to have relatives with past or present breast cancers compared with women with lower breast density [29, 30]. Our finding supports this with both lower density and fewer family histories of breast cancer reported for Aboriginal women. We also found that breast cancer in the family had significant multivariate association for non-Aboriginal women but not for Aboriginal women. This is unsurprising given the lower breast cancer incidence and lower rates of breast screening attendance in the Aboriginal population compared with the general population. Therefore, reports of family history of the disease are expected to be lower in the Aboriginal population.

The relationship between remoteness and density was only significant for non-Aboriginal women but not for Aboriginal women and it was not significant for all women grouped together. Non-Aboriginal women who were remotely located showed higher density than non-Aboriginal women living in outer regional areas. Consistent with national population data [20], there were more Aboriginal women living in remote to very remote locations compared with non-Aboriginal women in our sample. The higher fertility rate of remote-living Aboriginal women compared with Aboriginal women living in urban and regional areas [31], the younger age profile and the breastfeeding practices of Aboriginal mothers in general [32, 33] could potentially explain this result since parity, younger age at first birth, and breastfeeding have well-established associations with low density [34, 35]. Also, women living in Aboriginal communities which are mainly located in very remote regions of Australia would be less exposed to a range of other Westernised lifestyle factors that may have health impacts [36, 37].

Most non-Aboriginal women reported speaking predominantly English at home while most Aboriginal women mainly spoke Aboriginal languages. This is possibly linked with the prevalence of Aboriginal women living in remote to very remote locations where traditional languages are more likely to be spoken. According to census data [20], 15% of the general NT population speak Aboriginal languages and our result is a good representation of this with 15% of the women in our sample speaking Aboriginal languages. With regard to density, non-Aboriginal women with English-speaking background (ESB) showed stronger association with density than non-Aboriginal NESB women; however, when all women are considered, the variation in densities by ESB or NESB status was not significant. When all NESB women were further classified into either 'Aboriginal language' speakers or 'other non-English' speakers, the latter group showed higher probability of dense breasts compared with the former. Simply put, non-Aboriginal women who are not native English language speakers had higher density than their Aboriginal counterparts. In the NT, 19% of the population was born overseas and 15% speak in their native languages. While ethnicity and language use has been previously reported as an important determinant of density [24, 38], our results suggest that within NESB women, there is heterogeneity in terms of density and therefore stratifying women based on language and ethnic origin rather than considering them as a single non-English-speaking unit should be the focus of further work.

The association between HRT use and breast density is well-established [29, 39]. However, studies into the menopausal status and HRT use of Aboriginal women are globally scarce. While this study did not collect information on the menopausal statuses and types of HRT, our findings contribute to the currently limited knowledge of HRT use amongst Aboriginal Australians as compared with the non-Aboriginal population. Aboriginal women in our sample had a significantly lower rate of HRT use than non-Aboriginal women and the reasons for this could be similar to those reported in previous studies, those being, fear of using medication, an inclination towards coping with menopause symptoms naturally [40] and limited understanding of menopause, its symptoms and treatment options [41]. With regard to HRT use and density, univariate analyses found no significant associations for Aboriginal and non-Aboriginal women separately.

One of the disadvantages of a retrospective study such as this one is that some key variables cannot be measured because data were either not available or not routinely collected. While pathology data for this sample would be useful in showing how differences in density measures between groups of women in the NT relate to cancer detection and cancer risk, it must be noted that NT has the lowest breast cancer incidence in Australia (88 per 100,000 women vs. 115 per 100,000 nationwide) and invasive breast cancers in the Australian screening population is observed in 1 in every 200 cases [3]. Therefore, our sample (n = 4093) would potentially only yield a small number of cancer cases with low statistical power. To overcome this, further study using a larger sample size with high prevalence is warranted.

In addition to the absence of pathology data, menopausal status, and types of HRT as described above, a further limitation of this study is the lack of information on the body mass index (BMI) of individual women. As with age, body size is a critical predictor of breast density therefore adjustment for age and BMI is necessary [42]. Indeed, studies in the USA found that differences in breast densities across racial groups were significant when controlling for age and BMI [43, 44]. This critical variable could therefore impact the finding in this current work with the possibility of rendering significant associations null. With the reported difference between the body sizes of Aboriginal and non-Aboriginal women, in that Aboriginal women are 1.7 times more likely to have BMI >30.00 compared with non-Aboriginal women [5], we may have expected to see high BMI associated with increased non-dense area in the breast for Aboriginal women.

Furthermore, the absence of information regarding the reproductive histories of women and certain behaviours that have inverse associations with breast density such as smoking and physical activity limit the scope of this work These factors are particularly important since Aboriginal women are reported to be twice as likely as non-Aboriginal women to have a daily smoking habit with the highest rates in remote areas, have higher rates of fertility, and lower rates of physical activity [32]. Processes which enable a more comprehensive gathering of data related to breast density and breast cancer would facilitate greater epidemiological yield and should be explored.

Conclusion

This work has shown that for Aboriginal and non-Aboriginal women, younger age and being recalled to screening were strongly associated with density; however, for non- Aboriginal women, the following were additional covariates: HRT use, family history of breast cancer, remote residence, and language. We also reported significant differences in age profiles, geographical distribution, languages, HRT, and family histories of the disease between Aboriginal and non-Aboriginal women in the NT. This work contributes to the sparse literature on Aboriginal women in the BreastScreen NT population. With concomitant lower screening participation, younger age at diagnosis, and higher rates of death from breast cancer in Aboriginal women compared with non-Aboriginal women, a further key area of future study will be to explore if the differences in breast density are related to ethnic differences in breast cancer risk.

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References

1. Australian Institute of Health and Welfare, *BreastScreen Australia monitoring report 2009-2010*. 2012, AIHW.: Canberra, ACT. p. 93.

2. Chong, A. and D. Roder, *Exploring differences in survival from cancer among Indigenous and non-Indigenous Australians: implications for health service delivery and research.* Asian Pac J Cancer Prev, 2010. **11**(4): p. 953-61.

3. Australian Institute of Health and Welfare, *BreastScreen Australia monitoring report 2012–2013*. 2015, AIHW.: Canberra, ACT. p. 95.

4. Cancer Australia, *Study of breast cancer screening characteristics and breast cancer survival in Aboriginal and Torres Strait Islander Women of Australia*. 2012, Cancer Australia.: Surry Hills, NSW. p. 83.

5. Australian Institute of Health and Welfare, *The Health and Welfare of Australia's Aboriginal and Torres Strait Islander Peoples: 2015.* 2015, AIHW.: Canberra, ACT.

6. Australian Institute of Health and Welfare and Cancer Australia, *Cancer in Aboriginal and Torres Strait Islander peoples of Australia: an overview.* 2013, AIHW.: Canberra. p. 165.

7. Dasgupta, P., et al., *Multilevel determinants of breast cancer survival: association with geographic remoteness and area-level socioeconomic disadvantage.* Breast Cancer Res Treat, 2012. **132**(2): p. 701-10.

8. Gibberd, A., et al., *Are Aboriginal people more likely to be diagnosed with more advanced cancer?* Med J Aust, 2015. **202**(4): p. 195-9.

9. Shepherd, J.A. and K. Kerlikowske, *Do fatty breasts increase or decrease breast cancer risk?* Breast Cancer Research, 2012. **14**(1): p. 102.

10. Boyd, N.F., et al., *Mammographic density and the risk and detection of breast cancer.* N Engl J Med, 2007. **356**(3): p. 227-36.

11. Kerlikowske, K. and C.M. Vachon, *Breast Density: More Than Meets the Eye.* J Natl Cancer Inst, 2016. **108**(10).

12. American College of Radiology, *Breast Imaging Reporting and Data System Atlas (BI-RADS (Atlas)*. 2003, ACR: Reston, VA.

13. Roubidoux, M.A., et al., *Relationship of mammographic parenchymal patterns to breast cancer risk factors and smoking in Alaska Native women.* Cancer Epidemiol Biomarkers Prev, 2003. **12**(10): p. 1081-6.

14. Ursin, G., et al., *Mammographic density and breast cancer in three ethnic groups.* Cancer Epidemiol Biomarkers Prev, 2003. **12**(4): p. 332-8.

15. McCormack, V.A., et al., *Ethnic variations in mammographic density: a British multiethnic longitudinal study.* Am J Epidemiol, 2008. **168**(4): p. 412-21.

16. Ellison-Loschmann, L., et al., *Age and ethnic differences in volumetric breast density in new zealand women: a cross-sectional study.* PLoS One, 2013. **8**(7): p. e70217.

17. van der Waal, D., et al., *Comparing Visually Assessed BI-RADS Breast Density and Automated Volumetric Breast Density Software: A Cross-Sectional Study in a Breast Cancer Screening Setting.* PLoS One, 2015. **10**(9): p. e0136667.

18. Australian Bureau of Statistics, *1270.0.55.005 - Australian Statistical Geography Standard (ASGS): Volume 5 - Remoteness Structure, July 2011*. 2011, ABS: Canberra.

19. Barton, B., *Medical statistics : a guide to SPSS, data analysis and critical appraisal / Belinda Barton, Jennifer Peat*, ed. J.K. Peat. 2014, Chichester, West Sussex ; Hoboken, NJ: Wiley Blackwell/BMJ Books.

20. Australian Bureau of Statistics, *2075.0 - Census of Population and Housing - Counts of Aboriginal and Torres Strait Islander Australians, 2011*. 2011, ABS.: Canberra, ACT.

21. Roder, D., et al., *Breast screening and breast cancer survival in Aboriginal and Torres Strait Islander women of Australia.* Asian Pac J Cancer Prev, 2012. **13**(1): p. 147-55.

22. Pape, R., et al., *Mammographic parenchymal patterns and breast cancer risk in New South Wales North Coast Aboriginal and Torres Strait Islander women.* Journal of Medical Radiation Sciences, 2016. **63**(2): p. 81-88.

23. Boyd, N.F., et al., *Mammographic density and breast cancer risk: current understanding and future prospects.* Breast Cancer Res, 2011. **13**(6): p. 223.

24. Mariapun, S., et al., *Ethnic differences in mammographic densities: an Asian cross-sectional study.* PLoS One, 2015. **10**(2): p. e0117568.

25. Trieu, P.D.Y., et al., *Risk Factors of Female Breast Cancer in Vietnam: A Case-Control Study.* Cancer research and treatment : official journal of Korean Cancer Association, 2017. **49**(4): p. 990-1000.

26. Burton, A., et al., *Mammographic density and ageing: A collaborative pooled analysis of cross-sectional data from 22 countries worldwide.* PLoS medicine, 2017. **14**(6): p. e1002335-e1002335.

27. Al Mousa, D.S., et al., *How mammographic breast density affects radiologists' visual search patterns.* Acad Radiol, 2014. **21**(11): p. 1386-93.

28. AL Mousa, D.S., et al. *Mammographic Density Effect on Readers' Performance and Visual Search Pattern*. 2014. Cham: Springer International Publishing.

29. Boyd, N.F., et al., *Mammographic breast density as an intermediate phenotype for breast cancer.* The Lancet Oncology, 2005. **6**(10): p. 798-808.

30. Maskarinec, G., et al., *Ethnic and geographic differences in mammographic density and their association with breast cancer incidence.* Breast Cancer Res Treat, 2007. **104**(1): p. 47-56.

31. Johnstone, K., *Indigenous fertility in the Northern Territory of Australia: what do we know? (and what can we know?).* Journal of Population Research, 2010. **27**(3): p. 169-192.

32. Australian Bureau of Statistics, *4727.0.55.001 - Australian Aboriginal and Torres Strait Islander Health Survey: First Results, Australia, 2012-13*. 2013, ABS.: Canberra, ACT.

33. Smith, R.M., et al., *Birthweights and growth of infants in five Aboriginal communities.* Aust N Z J Public Health, 2000. **24**(2): p. 124-35.

34. Collaborative Group on Hormonal Factors in Breast Cancer, *Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 women without the disease.* The Lancet, 2002. **360**(9328): p. 187-195.

35. El-Bastawissi, A.Y., et al., *Reproductive and hormonal factors associated with mammographic breast density by age (United States).* Cancer Causes Control, 2000. **11**(10): p. 955-63.

36. O'Dea, K., *Diabetes in Australian aborigines: impact of the western diet and life style.* J Intern Med, 1992. **232**(2): p. 103-17.

37. Rowley, K.G., et al., *Effectiveness of a community-directed 'healthy lifestyle' program in a remote Australian aboriginal community.* Aust N Z J Public Health, 2000. **24**(2): p. 136-44.

38. Tehranifar, P., et al., *The metabolic syndrome and mammographic breast density in a racially diverse and predominantly immigrant sample of women.* Cancer Causes Control, 2015. **26**(10): p. 1393-403.

39. Greendale, G.A., et al., *Postmenopausal hormone therapy and change in mammographic density.* J Natl Cancer Inst, 2003. **95**(1): p. 30-7.

40. Jurgenson, J.R., et al., *Exploring Australian Aboriginal Women's experiences of menopause: a descriptive study.* BMC Women's Health, 2014. **14**(1): p. 47.

41. Davis, S.E., et al., *Climacteric symptoms among Indigenous Australian women and a model for the use of culturally relevant art in health promotion.* Menopause (New York, NY), 2003. **10**.

42. Huo, C.W., et al., *Mammographic density-a review on the current understanding of its association with breast cancer.* Breast Cancer Res Treat, 2014. **144**(3): p. 479-502.

43. del Carmen, M.G., et al., *Mammographic breast density and race.* AJR Am J Roentgenol, 2007. **188**(4): p. 1147-50.

44. McCarthy, A.M., et al., *Racial Differences in Quantitative Measures of Area and Volumetric Breast Density.* J Natl Cancer Inst, 2016. **108**(10).