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ORIGINAL ARTICLE

Mammographic parenchymal patterns and breast cancer risk in New South Wales North Coast Aboriginal and Torres Strait Islander women

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Aboriginal and Torres Strait Islander, breast cancer risk, breast density, mammographic parenchymal patterns, mammography screening

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Abstract

Introduction: The objective of the study was to document the distribution of mammographic parenchymal patterns (MPP) of Indigenous Australian women attending BreastScreen New South Wales (NSW) North Coast, to profile breast cancer risk as it relates to breast density and to explore the correlation between MPP, breast size as described by the posterior nipple line (PNL) and age. **Methods:** Ethics was granted from CQUniversity Human Research Ethics Committee, NSW Population Health Services Research Ethics Committee and the Aboriginal Health and Medical Research Council Ethics Committee. A quantitative retrospective analysis reviewed 502 screening mammograms against the Tabár I–V MPP classification system. The PNL was measured in millimetres (mm) and the age of the patient documented. **Results:** A statistically significant variation in the distribution of MPP ($P < 0.0001$) was demonstrated, with patterns of I (23.9%), II (45.6%), III (10.4%), IV (15.9%) and V (4.2%). Statistically significant differences were noted in the age of subjects between patterns ($P = 0.0002$). Patterns I and V demonstrated statistically significant lower ages than II, III and IV (all $P < 0.05$). Pattern V demonstrated a statistically significant lower age than pattern I ($P = 0.0393$). Pattern V demonstrated a statistically significant lower PNL value than all other patterns (all $P < 0.001/P < 0.0002$); pattern II was statistically significantly higher in PNL value than all other patterns ($P < 0.002/P < 0.001$). No significant relationship was noted between PNL and age. **Conclusion:** The study demonstrated that no identifiable or unique distribution of MPP was noted in this snapshot of Indigenous women. A larger study of Indigenous Australian women is required for validation.

Introduction

Breast cancer is a leading cause of mortality and morbidity worldwide, with a notable rise in incidence in developed nations such as Australia and New Zealand.[1] In response, population-based mammography screening programs for asymptomatic women were established globally and thus far have demonstrated a 15–20% relative reduction in breast cancer mortalities among women aged 40–74 years.[2] In Australia, the screening program BreastScreen Australia (BSA) has reduced breast cancer mortality nationally by approximately 21–28%.[3] At present the BSA program specifically targets asymptomatic women aged 50–74 years (an increase from 50 to 69 years since 2014); women aged 40–49 or 75 years and older are able to participate in the program, however they do not receive an invitation to screen.[4]

Excluding non-melanoma skin cancer, breast cancer is the most commonly diagnosed cancer among Indigenous and non-Indigenous Australian women.[5] Although Indigenous women have a lower incidence when compared to non-Indigenous Australian women, mortality rates are higher specifically for women aged 50–69 years.[6] Breast cancer survival reports between 2002 and 2006 have demonstrated the same, estimating a 5-year crude survival rate of 65% for Indigenous women compared to 82% for non-Indigenous women.[7–9] Indigenous survivals were lower across the entire BreastScreen target age group, regardless of sociodemographic factors including remoteness of residential location.[8] BSA data collected between 1996 and 2005 revealed a lower participation rate in screening mammography for Indigenous women compared to non-Indigenous women in the target age group (32% vs. 55%), which significantly improved to 36.5% between 2008 and 2009.[10]

Yet statistics suggest that Indigenous women have not benefited from breast screening (early detection) programs despite evidence showing participation as an effective way to reduce poor outcomes from breast cancer.[6] As such, decreased reported incidence may better reflect genetic, endogenous (early-onset menarche or late menopause), and exogenous (birthing history, breastfeeding frequency and duration) differences rather than lower effective participation rates in the BSA screening program.[6–8,10] Increased mortality and decreased survival figures may better reflect lifestyle differences (contraception use, diet, physical activity), overall poorer compliance with recommended treatment courses and higher levels of co-morbidities in the Indigenous population.[6–8,10,11]

Previous studies in numerous populations worldwide have demonstrated a positive correlation between particular mammographic parenchymal patterns (MPP), breast cancer incidence (BCI) and the risk of breast cancer development.[12–15] To date there are no reported studies identifying the distribution of MPP of Australian Indigenous women. It is possible that breast physiology among Indigenous women may be associated with lower BCI specifically as it relates to breast density and MPP. Considering the nominal benefits of breast screening programs for Indigenous women, investigation of MPP distribution and breast density as a risk factor for developing breast cancer is warranted in this population.

The aim of this study is to identify and document MPP distribution among Australian Indigenous women, specifically Aboriginal and Torres Strait Islander women,

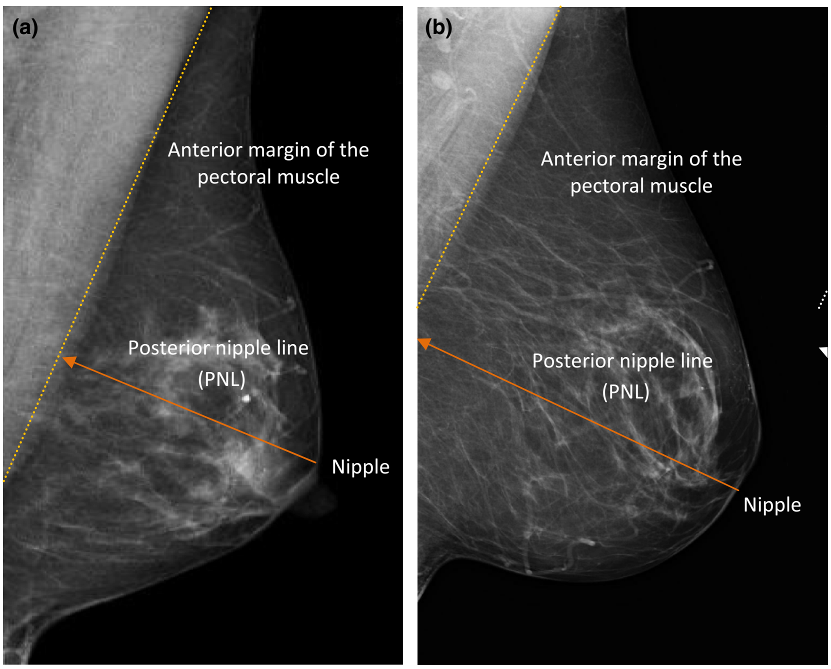

Figure 1. The posterior nipple line (PNL) is measured on the medio-lateral oblique (MLO) view of the breast as the distance from the nipple at right angles to the anterior margin of the pectoral muscle (a) or the posterior aspect of the image (b) whichever comes first.[16]

and establish a breast cancer risk profile as it relates to breast density in a population serviced specifically by BreastScreen New South Wales (NSW) North Coast. The correlation between MPP, age and breast length (size) as described by the image evaluation criterion, the posterior nipple line (PNL) will also be explored (Fig. 1). It is hypothesised that Australian Indigenous women have an identifiable and unique distribution of MPP and a breast cancer profile that indicates lower breast cancer risk.

The normal ductal and connective tissue patterns of the breast are depicted on a mammogram as various shades of grey representing variations in breast tissue density and referred to as MPP.[17] Classifying mammographic parenchymal tissue distribution serves two purposes: (1) to identify the ratio of dense to non-dense breast areas and (2) to estimate the risk of developing breast cancer.

There are currently four long-standing classification systems distinguished by their method of measuring MPP and breast density: the Wolfe, Tabár, Boyd and BI-RADS systems.[18–21] All categorise risk as high or low based on the calculated ratio of dense to adipose tissues. Higher ratios indicate increased density and overall greater risk for developing breast cancer, and vice versa. Evidence-based evaluations maintain the validity, reliability and usability of these classification systems to identify an overall risk profile in a healthy screening population.[15,22,23] The Tabár classification system describes five pattern types and has been chosen for this study as it is a highly reproducible and valid system, provided the reviewer has undergone appropriate training.[18,22,23]. The reviewer for this study is a qualified radiographer with several years of mammographic experience, and specific training in mammographic interpretation of MPP personally facilitated by Professor László Tabár, the system inventor. Each of the five patterns characteristics are described in Figures 2–6.

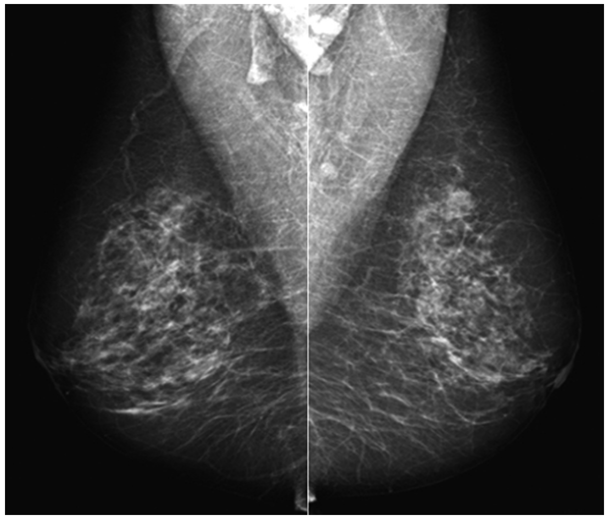

Figure 2. Mammographic parenchymal pattern I. Changes to either pattern II or pattern III with involution; is the most common mammographic parenchymal pattern in pre-menopausal women and is associated with an average risk for malignancy.[23]

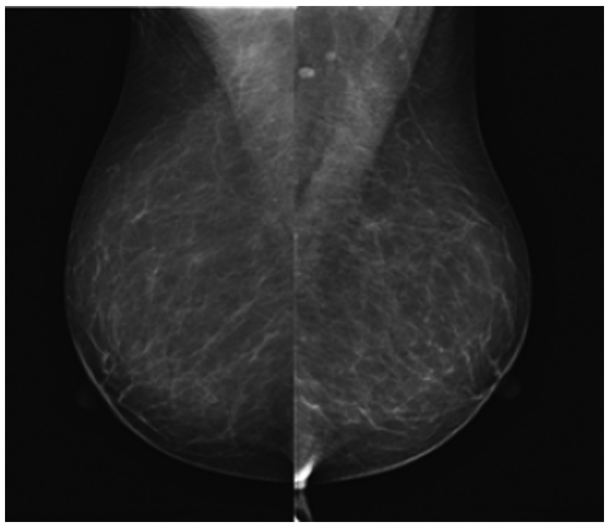

Figure 3. Mammographic parenchymal pattern II. Images are dominated by adipose tissue and linear densities representing the end-result of the process of involution. There is a low risk for malignancy.[23]

Materials and Methods

Ethics approval was granted from CQUniversity Human Research Ethics Committee (CQU HREC), NSW Population Health Services Research Ethics Committee (NSW PHSREC) and the Aboriginal Health and Medical Research Council Ethics Committee (AH&MRC EC).

A quantitative retrospective analysis of 502 paired screening cranio-caudal (CC) and medio-lateral oblique (MLO) mammograms of Indigenous Australian women who attended screening at BreastScreen NSW North Coast between 1 July 2010 and 30 June 2012 and self-identified as of Aboriginal and Torres Strait Islander ethnicity on the Screening Consent Form (SCF) was performed.[25] These dates were chosen to maximise sample size as women typically undergo screening every 2 years and to ensure all images were produced by the same technology. Women who had undergone mastectomy, radiation therapy, breast augmentation or presented with chest wall deformity or shoulder injury were excluded from the study. Classification of the mammographic images using Tabár MPP categories I–V was performed by direct observation. Each paired set of images was independently and blindly reviewed three times. Discrepancy was addressed by consensus.

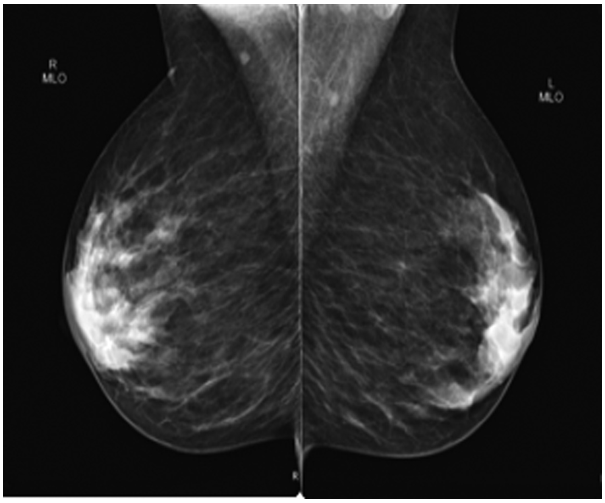

Figure 4. Mammographic parenchymal pattern III. Similar to Pattern II with the exception of the prominent retroareolar duct pattern. This is a characteristic presentation in older women and is associated with a low risk of malignancy.[23]

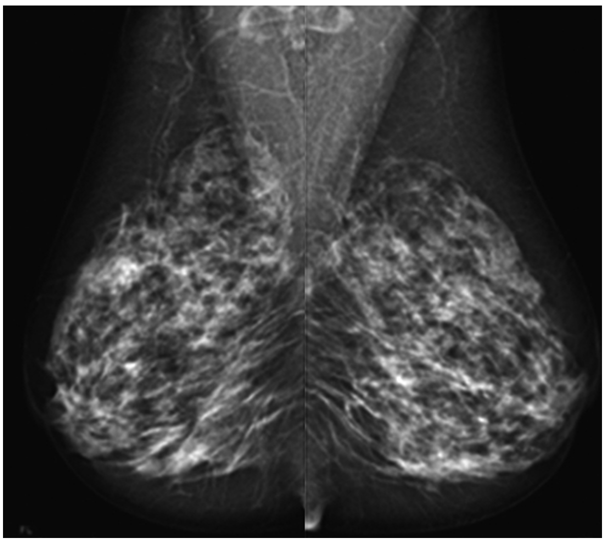

Figure 5. Mammographic parenchymal pattern IV. Images are dominated by prominent nodular densities that correspond to enlarged terminal ductal lobular units, (TDLU's) and linear densities. Perception of pathological lesions is difficult and this mammographic parenchymal patterns (MPP) often remains unaltered with time. There is a high risk for malignancy.[23]

The PNL on the MLO view was measured in millimetres (mm) as the distance from the nipple at right angles to the anterior margin of the pectoral muscle or the posterior aspect of the image[16] (see Fig. 1). The PNL measurement is not a literal measurement, but is used in this study to facilitate discussion around breast size.

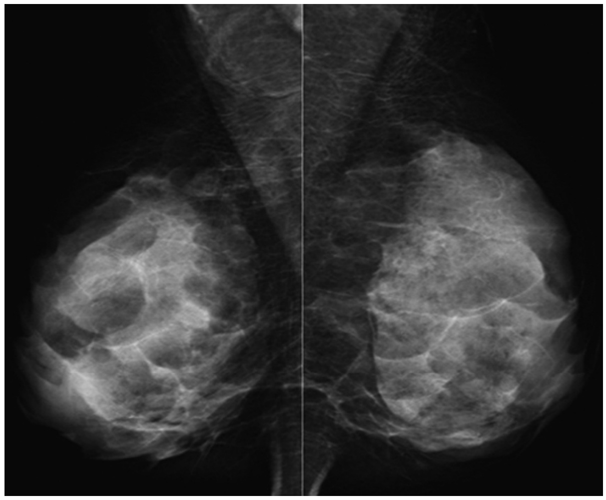

Figure 6. Mammographic parenchymal pattern V. The predominance of homogeneous, structureless fibrous tissue limits the capabilities of mammography as a screening tool. There is a high risk for malignancy.[23]

Statistical analysis

Statistical analysis evaluated the relationship between Tabár patterns I–V, age and PNL. Left versus right PNL and PNL versus age was also analysed. Statistical significance was calculated using chi-square analysis for nominal data and Student's *t*-test for continuous data. The likelihood ratio chi-square (G^2) test analysed categorical data without normal distribution. The *F*-test analysis of variances was used to determine statistically significant differences within grouped data. A *P*-value less than 0.05 was considered significant. The Shapiro–Wilk *W* test with a *P*-value less than 0.05 indicated that the data vary significantly and were not normally distributed.

Differences between independent means and proportions were calculated with a 95% confidence interval (CI). CI's without an overlap and/or those which did not include zero supported a statistically significant difference while CI's with an overlap and/or those that included zero represented differences in which chance could not be excluded as the cause.

Results

There was limited discrepancy in the assigning of MPP categories with very few images being assigned to two pattern types. No images were assigned more than two pattern types suggesting limited observer bias within images. Age was normally distributed within the 502 participants and ranged from 40 to 78 years with a mean age of 57 years.

Table 1. Distribution of breast parenchymal tissue patterns (I–V).

MPP (I–V)	Number of Aboriginal and Torres Strait women	% of total Aboriginal and Torres Strait women per pattern	% Tabár study results[18]
Pattern I – scattered fibroglandular densities (average density)	120	13	23.9
Pattern II – predominantly adipose tissue (low density)	229	42.1	45.6
Pattern III – predominantly adipose tissue (low density)	52	26.9	10.4
Pattern IV – heterogeneously dense (high density)	80	12	15.9
Pattern V – extremely dense (very high density)	21	6	4.2
Total	502	100.0	100.0

MPP, mammographic parenchymal patterns.

The distribution of Tabár MPP is summarised in Table 1. A statistically significant variation between the distribution in the study population and the standard expected Tabár distribution was noted ($P < 0.0001$).[18] This reflects a greater representation of the study population in pattern I and fewer in pattern III.

The mean left PNL was 132.91 mm (95% CI: 129.94–135.88 mm) with a range of 50.83–265.36 mm and median of 130.73 mm. The mean right PNL was 133.42 mm (95% CI: 130.45–136.39 mm) with a range of 44.14–253.53 mm and median of 131.95 mm. Both left and right PNL were normally distributed. No statistically significant difference was noted between the mean data for left and right PNL ($P = 0.7365$) as supported by the overlap of the 95% CIs. The mean difference between paired data for the right and left PNL was 0.508 mm (95% CI: −0.193–1.211 mm) with the matched pairs *t*-test indicating no statistically significant difference ($P = 0.9224$) with a strong correlation coefficient (0.972).

A statistically significant difference was noted in the grouped data between the age of subjects and the Tabár patterns ($P = 0.0002$) (see Fig. 7). While no statistically significant differences were noted among Tabár patterns II, III and IV ($P > 0.500$), patterns I and V demonstrated statistically significant lower ages than II, III and IV (all $P < 0.05$). This is despite a small overlap in 95% CIs for pattern I and II and between patterns III and IV. Furthermore, pattern V demonstrated a statistically significant lower age than pattern I ($P = 0.0393$).

Statistically significant differences were also noted in the left PNL between Tabár patterns ($P < 0.0001$) (see Fig. 8). While no statistically significant differences were noted among Tabár patterns I and III ($P = 0.832$), statistically significant differences were noted between all other patterns (all $P < 0.05$). Of particular note was that, pattern IV demonstrated a statistically significant lower PNL all other patterns (all $P < 0.001$) and pattern II was statistically significantly higher in PNL than all other patterns ($P < 0.002$).

The same pattern was noted for the right PNL with statistically significant differences noted between Tabár patterns ($P < 0.0001$) (see Fig. 9). While no statistically significant differences were noted among Tabár categories I and III ($P = 0.754$) and III and IV ($P = 0.064$), statistically significant differences were noted between all other categories (all $P < 0.05$). Of particular note was that, category V demonstrated a statistically significant lower PNL than all other patterns (all $P < 0.0002$) and category II was statistically significantly higher in PNL than all other categories ($P < 0.001$).

No statistically significant relationship was noted between age and PNL for either left ($P = 0.365$ with R^2 of 0.001) or right ($P = 0.568$ with R^2 of 0.0006).

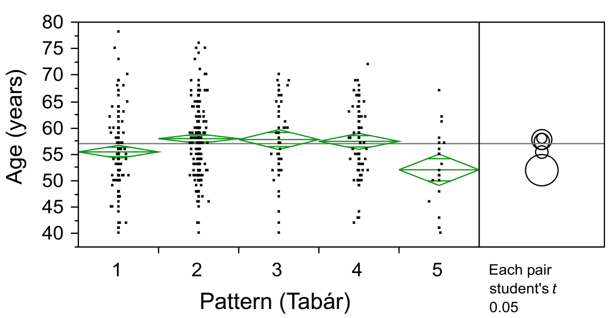

Figure 7. Age versus patterns I–V.

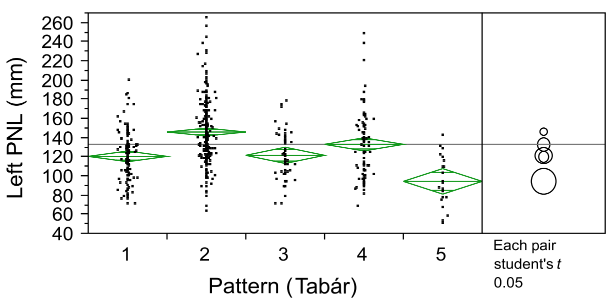

Figure 8. One-way analysis of left posterior nipple line (PNL) (mm) against Tabár patterns I–V.

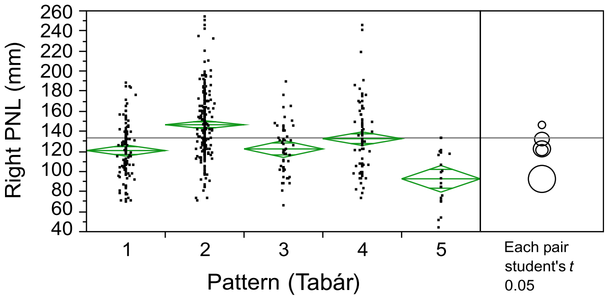

Figure 9. One-way analysis of right posterior nipple line (PNL) (mm) against patterns I–V (Tabár).

Discussion

Analysis of MPP has shown value in terms of predicting breast cancer in women including women of specific population groups.[26] Such analysis allows high-risk mammographic patterns including patterns IV, V and occasionally pattern I to be flagged[27,28] and recommended for adjunct imaging such as ultrasound or magnetic resonance imaging.[29–31]

Women with patterns IV and V are categorised as high risk and are twice more likely to develop breast cancer than women with low-risk patterns I and II.[17,24,32] Low-risk patterns were identified in 79.9% of participants, closely reflecting the defined Tabár MPP distributions (82%) (see Table 1).[17,24] Low-density breasts have a greater proportion of adipose tissue resulting in more confident mammographic interpretation.

The remaining patterns (20.1%) represented women with high-risk MPP's at a rate greater than the defined Tabár MPP distributions (18%) (see Table 1), though not statistically significant. The low frequency of dense breasts (20.1%) in the current study differs from other ethnic populations, particularly women of Asian descent who have documented frequencies as high as 76%.[14,33]

Additional predictive independent risk factors include age and hormonal status.[34,35] Breast density is inversely related to age and directly influences the MPP visualised in a general screening population.[36,37] Age is also associated with hormonal status, specifically pre- or post-menopausal status and hormone replacement therapy use. Results of this study support existing evidence that breast density typically decreases with age due to hormonal factors. The denser MPP I and V had a statistically significant association with younger women than MPP II, III and IV (all $P < 0.05$); this finding is therefore expected. This was particularly the case for pattern V which demonstrated a statistically significant lower age than pattern I ($P = 0.0393$) (Fig. 7).

The current study demonstrated no statistically significant relationship between age and breast size based on the PNL criterion for either the left or right breast, a finding that is supported by Hoe et al. who reported breast size to be independently associated with age and not a significant prognostic factor in women with early breast cancer.[38] This is to be expected as breast size is not a function of age after reproductive maturation. PNL measurements were normally distributed and there was no statistically significant difference between the left and right breast values demonstrating that human breasts are mostly symmetrical.[39]

Analysis of breast size (PNL) and pattern reflected the ratio of adipose-to-glandular tissue and its influence on breast size. Of particular note was that, category V demonstrated a statistically significant lower PNL than all other patterns (all $P < 0.0002$) and category II was statistically significantly higher in PNL than all other categories ($P < 0.001$). Larger breasts inherently have a greater volume of adipose tissue as compared to smaller breasts demonstrating that a greater adipose-to-glandular tissue ratio is typically associated with larger breasts.

The Indigenous Australian women selected for this study represent a snapshot of the national Indigenous population of Australia limiting generalisation. Images were also chosen based on self-identification as Indigenous at the time of screening and the true Indigenous population may not have been fully represented in this study.[40] Local women screened by BreastScreen NSW North Coast typically identify with the Birpai, Bundjalung, Daingutti, Githabul, Gumbaynggirr and Yaegl Nations, though participation from other nations cannot be excluded.

All mammographic images were interpreted by a single qualified radiographer with several years of mammographic experience and specific training in mammographic MPP interpretation. The researchers acknowledge the potential for biased variability of qualitative MPP measurement.

Conclusion

The aim of this study was to document the MPP of Indigenous Australian women and the relationship with breast cancer risk. There are no identifiable or unique MPP to support greater risk of cancer among Indigenous Australian women in this sample. Without statistical evidence to support decreased breast density, it can be postulated that endogenous and exogenous factors may better reflect the lower incidence of breast cancer. Lifestyle differences, greater co-morbidities and lower effective participation rates in the BSA screening program may better explain higher mortality in this population. A larger and more comprehensive national study of the Aboriginal and Torres Strait Islander population is required to validate these findings.

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Conflict of Interest

The authors declare no conflict of interest.

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