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Effectiveness of adjunctive ultrasound after mammography in improving breast cancer screening findings from a study in Malaysian women

Mohamed Ibrahim Wahid[1], Nurul Alia Azmi[2], Pei Yun Tan[3], Bao Jing Chen[4]

[1]Consultant Clinical Oncologist, Department of Oncology, [2,3]Clinical Research Analyst, [4]Head, Department of Clinical Research, Beacon Hospital, Selangor, Malaysia

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ABSTRACT

Background: Breast cancer is a significant health issue affecting women worldwide, including Malaysia, where the incidence of breast cancer is increasing. Early detection of breast cancer plays a crucial role in improving treatment outcomes and reducing mortality rates. **Aims and Objectives:** This study examines the impact of adjunctive breast ultrasound (BUS) on screening for Malaysian women, offering evidence to enhance future protocols and decisions in the early detection. **Materials and Methods:** This study involved 5807 women aged 40 and above undergoing breast screening at Beacon Hospital from January to December 2022. Data collected included mammography and BUS results, categorized by breast imaging reporting and data system (BI-RADS) and diagnostic criteria. Suspicious cases on both modalities had histopathology examination (HPE) for confirmation. A subset of 1690 cases underwent both mammography and BUS screening and was compared to those who only had mammography using BI-RADS scores. **Results:** This study revealed that the majority of mammograms, 94.69% (5499 cases), were categorized as BI-RADS category 0, 1, 2, and 3, while 5.3% (307 cases) were classified as BI-RADS 4 and 5. Among the cases that underwent ultrasound (1688 cases), 23.43% of them were categorized as BI-RADS 4–5. Using ultrasound in addition to mammography increased the number of cases (BI-RADS 4–5) by 33.48%, resulting in a total of 460 cases identified compared to 307 cases, detected by mammography alone. Significantly, 39% (74 cases) of the 190 cases with confirmed malignancies (BI-RADS 6) by HPE were initially classified as negative mammography (BI-RADS 0–3) but were later identified as BI-RADS 5 on ultrasound. **Conclusion:** Ultrasound as a supplementary screening method holds the potential for boosting breast cancer detection sensitivity and reducing false negatives, thereby aiding in early detection and better treatment outcomes.

Key words: Breast Cancer; Screening; Ultrasound

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INTRODUCTION

Breast cancer is a significant health issue affecting women worldwide, including Malaysia, where the incidence of breast cancer is increasing.[1] According to the Malaysia National approximately 1 in 19 Malaysian women are diagnosed with breast cancer.[2] Early detection of breast cancer plays a crucial role in improving treatment outcomes and reducing mortality rates.[3] Mammography has been widely used as the primary screening tool for breast cancer, enabling the detection of abnormalities such as tumors at an early stage.[4] However, its effectiveness may be limited in women with dense breast tissue.

Dense breast tissue is characterized by a higher proportion of fibrous and glandular tissue, which appears white on

Address for Correspondence:
Dr. Mohamed Ibrahim Wahid, Consultant Clinical Oncologist, Department of Oncology, Beacon Hospital, Selangor, Malaysia.
Mobile: +60376207979/+60377872992. **E-mail:** dribrahim@beaconhospital.com.my

mammograms, making it challenging to differentiate between normal breast tissue and potential tumors, which also appear white.[5] This density can obscure small lesions and decrease the sensitivity of mammography, leading to a higher rate of false-negative result.[6] Women with dense breasts are at an increased risk of developing breast cancer, and the limitations of mammography in this population have prompted the exploration of adjunctive screening techniques.

Breast ultrasound (BUS) has emerged as a promising adjunctive screening modality for breast cancer, particularly in women with dense breast tissue.[7] BUS uses sound waves to create images of the breast tissue, providing a complementary approach to mammography. It offers several advantages, including the ability to visualize breast abnormalities in detail, distinguish between solid masses and fluid-filled cysts, and assess the vascularity of lesions.[8]

The use of BUS as an adjunct to mammography has been proposed to improve the detection of breast cancer in women with dense breasts. By combining the two modalities, it is possible to enhance the sensitivity of screening and identify abnormalities that may have been missed by mammography alone.[9] However, the effectiveness of adjunctive BUS after mammography in improving breast cancer screening outcomes, particularly in the context of Malaysian women, requires investigation.

Aims and objectives

Therefore, the data were collected at Beacon Hospital in Selangor, Malaysia, aimed to evaluate the effectiveness of adjunctive BUS following mammography in improving breast cancer screening outcomes, with a specific focus on the population of Malaysian women. By assessing the benefits of combining mammography and BUS, the study aimed to identify optimal screening strategies that could be applicable not only to Malaysian women but also to women worldwide, ultimately reducing false-negative results and improving early detection of breast cancer.

MATERIALS AND METHODS

Study design

The retrospective study was conducted over a 1-year period, specifically from January 1, 2022, to December 31, 2022. During this time, a comprehensive investigation was carried out at Beacon Hospital involving a total of 5807 eligible women aged 40 years old and above who presented for breast screening.

To assess the effectiveness of adjunctive BUS in improving breast cancer screening outcomes, a subset of cases (n=1690) underwent BUS screening in addition to mammography. The sample size was determined based on factors such as the desired margin of error, the population size, and the confidence level within the population. These factors were considered to ensure that the sample size was sufficient to detect meaningful differences and provide reliable results. This subset represented a portion of the overall study population and was specifically chosen to investigate the potential benefits and impact of incorporating BUS into the screening protocol, with the findings informing future screening strategies and protocols for Malaysian women and potentially women worldwide.

Data collection

Data collection for the study involved obtaining and recording information from imaging examinations, specifically mammography and BUS. Detailed observations were made, including the assessment of mammography density. The diagnostic results from BUS were categorized into five groups: (1) Normal, (2) benign, (3) probably benign, (4) suspicious malignancy, and (5) highly suspicious. Similarly, the mammogram results were evaluated according to the breast imaging reporting and data system (BI-RADS) categories established by the American College of Radiology. These BI-RADS categories included: (0) Additional imaging needed, (1) negative, (2) benign, (3) probably benign, (4) suspiciously malignant, and (5) highly suggestive of malignancy. For the purposes of the study, BI-RADS categories 4–5 were considered positive findings, while all other diagnostic results were considered negative. Ethics approval was obtained from the Medical Research Ethics Committee (MREC ID: NMRR ID-23-02627-0RJ).

For participants who had suspicious findings on both mammography and BUS, a histopathology examination (HPE) of breast tissue was conducted. The HPE reports were then used to confirm the presence of breast cancer in cases where malignancy was identified. This step served as the definitive method to validate the diagnosis of breast cancer based on histopathological evidence.

Statistical analysis

Data analysis was performed to examine the distribution of BI-RADS categories for both mammography and BUS. Descriptive statistics, including counts and percentages, were calculated to summarize the data and identify patterns. Detection rates were calculated for each screening modality group.

To investigate associations between variables, statistical tests such as the t-test, Chi-square test, or Fisher's exact test were employed. These tests were used to determine if there were significant relationships or differences in the distribution of BI-RADS categories between mammography and BUS, as well as to explore associations between other relevant variables.

The SPSS statistic version 23.0 software (IBM SPSS Inc., USA) was used for data processing and analysis. A two-sided P<0.05 was considered statistically significant, indicating a significant association or difference between variables.

RESULTS

A total of 5807 eligible women were included in the study, with a mean age falling within the range of 40–50 years. The study revealed that the majority of mammography, 94.69% (5499 cases), were categorized as BI-RADS Category 0, 1, 2, and 3, indicating a low suspicion for malignancy, while 5.3% (308 cases) were classified as BI-RADS 4 and 5 suggesting a moderate to high suspicion for malignancy. In the subset of cases (n=1690) that underwent BUS screening in addition to mammography, 23.43% (n=396) were classified as BI-RADS 4–5, indicating a moderate to high suspicion for malignancy (Table 1).

Incorporating BUS alongside mammography led to a 33.48% rise in the number of cases classified as BI-RADS 4–5. This resulted in a total of 460 cases being identified with adjunct BUS, in contrast to the 307 cases detected by mammography only (Figure 1).

In our study, the addition of BUS to the screening process led to a significant increase in the detection rate of suspicious cases with BI-RADS 4–5. Specifically, we observed that 153 cases initially classified as negative on mammogram, BI-RADS 0–3 were later identified as BI-RADS 4–5 on BUS. In addition, among these 153 cases, 62.74% (n=96) had breast density categorized as C and D, indicating mammographic breast density >50% (Table 2).

Among the 1690 incidence, 190 women were diagnosed with cancer. For incidence screening, the sensitivity of combined mammography and BUS was 116 of 190 (0.61; 95% CI, 0.53–0.70), higher than mammography alone, which was 74 of 190 (0.39; 95% CI, 0.31–0.47; P<0.01). The 74 cases initially classified as false-negative, where results in breast cancer screening occur when a mammogram fails to detect a breast cancer that is actually present on BUS (Table 3).

In addition, our study also looked at women age below 50 which patients may be pre- or perimenopause. Thirty-five (19.4%) patients under the age of 50 were classified as BI-RAD 4–5 based solely on mammogram results, whereas 180 patients received the same classification based on both mammogram and ultrasound findings. Among these, there were 141 patients had breast density categorized as C and D. For the age above 50, 30 (13.9%) patients were classified as BI-RAD 4–5 based solely on mammogram results, whereas 216 patients received the same classification based

Table 1: Number of cases of BI-RADS assessment using mammography and mammography with BUS

BI-RADS category	Mammography (%) (n=5806)	Mammography with BUS (%) (n=1690)
0	1302 (22.4)	
1	1253 (21.6)	373 (22.1)
2	2504 (43.1)	608 (36)
3	440 (7.6)	313 (18.5)
4	140 (2.4)	156 (9.2)
5	168 (2.9)	240 (14.2)

BI-RADS: Breast imaging reporting and data system, BUS: Breast ultrasound

Table 2: Distribution of cases based on breast density categories that identified as BI-RADS 0-3 on mammogram were later identified as BI-RADS 4 and 5 on adjunct BUS

Breast density	Cases identified as BI-RADS 4–5 in adjunct BUS
A	3
B	39
C	58
D	38
Unknown	15

BI-RADS: Breast imaging reporting and data system, BUS: Breast ultrasound

Table 3: Sensitivity of mammography and adjunct BUS compared with mammography alone in women diagnosed with cancer

Test	Sensitivity (95% CI)
Mammography	0.39 (0.31, 0.47)
Mammography+BUS	0.61 (0.53, 0.70)
P	P<0.01

BUS: Breast ultrasound

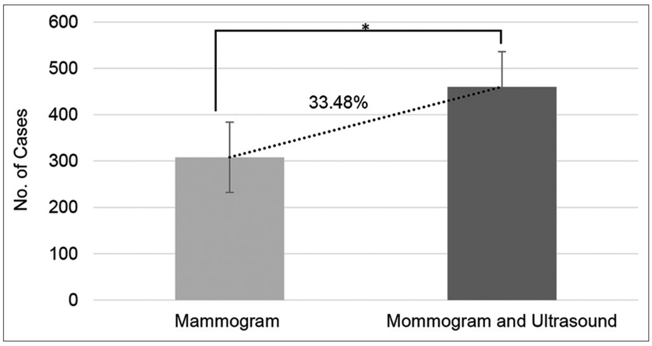

Figure 1: Number of cases with breast imaging reporting and data system 4 and 5 between mammogram only and mammogram adjunct with ultrasound. The asterisk (*) shows a significant difference (P<0.05) between patients (breast imaging reporting and data system 4 and 5) that took mammogram only and ultrasound in addition to mammogram

Table 4: Distribution of participants based on adjunctive BUS and mammography results

MAM	BUS (-ve)	BUS (+ve)
	Number of participant	Number of participant
MAM (-ve)		
BI-RADS 0	450	129
BI-RADS 1	155	2
BI-RADS 2	504	14
BI-RADS 3	185	8
MAM (+ve)		
BI-RADS 4		105
BI-RADS 5		138

BI-RADS: Breast imaging reporting and data system, BUS: Breast ultrasound

Table 5: The sensitivity of detecting breast cancer when adjunctive breast ultrasound is combined with mammography compared to mammography alone, based on different studies

References	Mammography (%)	Adjunctive BUS with Mammography (%)
13	32.6	48.8
14	50	77.5
15	40	81
Current study	39	61

BUS: Breast ultrasound

on both mammogram and ultrasound findings. There were 120 patients who had breast density categorized as C and D.

DISCUSSION

Mammography has long been considered the gold standard for breast cancer screening, contributing to the early detection of breast cancers and saving lives. However, it is important to acknowledge that mammography has limitations. Our study addresses these limitations and provides compelling evidence for the integration of BUS as a complementary screening modality to improve the detection of suspicious breast lesions. In our study, we observed an increase in the number of cases in the detection of cases categorized as BI-RADS 4–5 when BUS was added to mammography (Table 1). These findings are consistent with previous research that has highlighted the limitations of mammography as a standalone screening tool.[10,11]

Furthermore, our study demonstrates the valuable role of BUS in improving the detection of suspicious breast lesions beyond what mammography can achieve alone. By incorporating adjunctive BUS following mammography, we identified 9% (n=153 out of 1688) of cases initially classified as negative BI-RADS (BI-RADS 0–3) on mammography that were later reclassified as positive BI-RADS (BI-RADS 4–5) on BUS, indicating the presence of suspicious lesions (Table 4). This highlights the additional diagnostic value provided by BUS, enabling the identification of lesions that might have been missed by mammography alone.

The integration of BUS as an additional screening tool helps overcome the limitations of mammography, especially in cases where mammography exhibits lower sensitivity. By utilizing both modalities, radiologists can improve the detection of suspicious lesions, leading to earlier diagnoses and potentially improved patient outcomes. The previous studies have also supported the use of BUS in combination with mammography, highlighting its role in enhancing detection.[12,13] Our study provides strong evidence supporting the significant improvement in breast cancer detection sensitivity achieved by incorporating BUS as an adjunctive screening modality. Consistent with previous research conducted by.[13,14] and[15] found a notable increase in sensitivity ranging from approximately 16% to 41% when BUS is used in conjunction with mammography compared to mammography alone (Table 5).

In our specific study, we observed a clear and consistent trend of improved detection rates of breast cancer with the addition of BUS. When mammography was used as the sole screening method, it detected 12.7 cases of breast cancer per 1000 women screened. However, when BUS was incorporated as an adjunctive tool to mammography, the detection rate significantly increased to 19.9 cases per 1000 women screened ($P<0.05$). This stark contrast highlights the substantial impact of integrating BUS into the screening process and underscores its crucial role in achieving more accurate and comprehensive detection of breast cancer.

In addition, mammography faces a significant challenge in effectively detecting breast lesions in women with dense breast tissue. Dense breast tissue can mask abnormalities on mammogram, making them difficult to accurately discern. This masking effect poses a considerable problem for breast cancer detection as it can result in false-negative results, where a mammography fails to detect a breast cancer that is actually present. Our study findings align with this challenge, as we observed a high percentage of false-negative results in patients with dense breasts. Approximately 73% of the false-negative cases in our study were attributed to the presence of dense breast tissue. This further emphasizes the need for additional screening approaches for women with dense breasts. In women with dense breasts, tumors or suspicious lesions may be obscured by the overlapping glandular tissue, reducing their visibility on mammographic images. Consequently, there is an increased risk of breast cancer going undetected, potentially leading to delays in diagnosis and treatment.[6]

Numerous studies evaluating the effectiveness of combining BUS with mammography consistently demonstrate that BUS enhances the detection of suspicious breast lesions, particularly in women with dense breast tissue.[14,13] BUS provides valuable additional information beyond what is captured by mammography alone. It offers visualizations of additional features such as lesion shape, size, vascularity, and internal architecture, allowing for a more comprehensive evaluation of breast abnormalities that may have been missed on mammogram, thereby increasing the detection rate of suspicious lesions.[14,13] This additional information aids in differentiating between benign and malignant lesions, thereby improving diagnostic accuracy. Our own investigation confirmed these findings, as we observed an increased susceptibility to false-negative results on mammogram in the presence of dense breast tissue (Table 2). Recent research by[10] aligns with our study, demonstrating the limitations of mammography in dense breast tissue and highlighting the potential consequences of false-negative results. There are research indicates that Asian women have been consistently reported to have denser breast compared to Caucasian women.[16] These findings further support the need for improved screening approaches for women with dense breasts.

The integration of BUS into breast cancer screening protocols addresses the limitations of mammography in individuals with dense breast tissue. By providing additional imaging information, BUS offers a non-invasive and complementary approach to detect abnormalities that may be obscured by dense tissue on mammogram. This combination improves the accuracy of breast cancer diagnosis and enhances the likelihood of timely detection, ultimately leading to more effective treatment and improved patient outcomes. Nevertheless, it is crucial to acknowledge that the integration of BUS as a routine screening tool requires further evaluation, including considerations of long-term outcomes, cost-effectiveness, and feasibility.

CONCLUSION

Our study provides strong evidence supporting the integration of BUS as an adjunctive screening modality to improve breast cancer detection, particularly in women with dense breast tissue. By combining BUS with mammography, we observed a significant increase in the detection rate of suspicious cases beyond what mammography alone can achieve. This finding highlights the limitations of mammography in effectively detecting breast lesions in women with dense breasts and emphasizes the need for additional screening approaches.

The addition of BUS to the screening process offers several advantages, including enhanced sensitivity in detecting suspicious lesions and improved diagnostic accuracy. Our study demonstrated a clear and consistent trend of improved detection rates when BUS was incorporated, further corroborating previous research that has advocated for the use of BUS as a complementary tool to mammography.

Limitations of the study

Breast cancer is a condition that may take years to manifest and a 1-year study duration might not capture the long-term effectiveness and outcomes associated with adjunctive BUS. The cost-effectiveness of incorporating BUS into routine screening protocols was not evaluated in this study. Considering the potential impact on healthcare costs and resource utilization is crucial for the practical implementation of new screening technologies.

While our study provides valuable insights into the effectiveness of adjunctive BUS, further research is needed to evaluate long-term outcomes, cost-effectiveness, and the feasibility of integrating BUS into routine breast cancer screening protocols. In addition, future studies should explore the potential impact of BUS on reducing mortality rates and improving overall survival.

In conclusion, the integration of BUS as an adjunctive screening modality shows promise in improving breast cancer detection, particularly in women with dense breast tissue. By enhancing the sensitivity of screening and reducing false-negative results, BUS has the potential to contribute significantly to early detection and improved treatment outcomes. Further research and evaluation are necessary to fully understand the benefits and challenges associated with incorporating BUS into routine breast cancer screening practices.

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Authors Contributions:
DMIW- Conceptualization, supervision and final approval; **NAA-** Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis; **PYT-** Manuscript preparation, editing, manuscript revision, statistical analysis and interpretation and submission of article; **BJC-** Review Manuscript.

Work attributed to:
Beacon Hospital Breast Clinic and Clinical Research Department.

Orcid ID:
Mohamed Ibrahim Wahid - https://orcid.org/0009-0003-1199-2308
Nurul Alia Azmi - https://orcid.org/0009-0008-5959-3935
Pei Yun Tan - https://orcid.org/0009-0007-7017-8137
Bao Jing Chen - https://orcid.org/0009-0000-8697-4663

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