The Comparative Accuracy of Ultrasound and Mammography in The Detection of Breast Cancer

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SUMMARY

Aim: This study was performed to determine the accuracy of ultrasound (USG) as compared to mammography (MMG) in detecting breast cancer.

Methods: This was a review of patients who had breast imaging and biopsy during an 18-month period. Details of patients who underwent breast biopsy were obtained from the department biopsy record books and imaging request forms. Details of breast imaging findings and histology of lesions biopsied were obtained from the hospital Integrated Radiology Information System (IRIS). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of USG and MMG were calculated with histology as the gold standard.

Results: A total of 326 breast lesions were biopsied. Histology results revealed the presence of 74 breast cancers and 252 benign lesions. USG had a sensitivity of 82%, specificity of 84%, PPV = 60%, NPV = 94% and an accuracy of 84%. MMG had a sensitivity of 49%, specificity of 89%, PPV = 53%, NPV = 88% and an accuracy of 81%. A total of 161 lesions which were imaged with both modalities were analyzed to determine the significance in the differences in sensitivity and specificity between USG and MMG. Sensitivity of USG (75%) was significantly higher than sensitivity of MMG (44%) (X^2_1=6.905, p=0.014). Specificity of MMG (91%) was significantly higher than specificity of USG (79%) (X^2_1=27.114, p<0.001). Compared with MMG, the sensitivity of USG was 50% (95% CI 10%-90%) higher in women aged less than 50 years (X21=0.000, p=1.000) and 27% (95% CI 19%-36%) higher in women aged 50 years and above (X^2_1=5.866, p=0.015). Compared with MMG, the sensitivity of USG was 40% (95% CI 10%-70%) higher in women with dense breasts (X^2_1=0.234, p=0.628) and 27% (95% CI 9%-46%) higher in women with non-dense breasts (X^2_1=4.585, p=0.032).

Conclusion: Accuracy of USG was higher compared with MMG. USG was more sensitive than MMG regardless of age group. However, MMG was more specific in those aged 50 years and older. USG was more sensitive and MMG was more specific regardless of breast density. In this study, 20% of breast cancers detected were occult on MMG and seen only on USG.

KEY WORDS:
Breast cancer, ultrasound, mammography, accuracy, sensitivity.

INTRODUCTION

The value of mammography (MMG) in the detection of early breast cancer has long been established. Several randomised clinical trials have proven that screening MMG have reduced mortality rates from breast cancer by 15-22%[1]. But MMG has its limitations. The false negative rate of MMG can be as high as 35%[2]. Possible causes of breast cancers missed on MMG include dense breast parenchyma obscuring a lesion, suboptimal positioning or technique, perception error, incorrect interpretation of a suspect finding, and subtle features of malignancy[2]. While most of these causes can be overcome with adequate training and experience, the problem with dense breast parenchyma raises the need for other imaging methods such as breast ultrasound (USG) to supplement MMG.

The majority of Malaysian women have dense breasts on MMG[3, 4]. This could lead to a higher likelihood of missing a lesion. At our centre, USG is performed to further evaluate breasts that are dense on MMG. Apart from this, our centre advocates the use of USG to evaluate (i) an abnormality detected on MMG, (ii) breast(s) and bilateral axilla of women with personal history of breast cancer with normal MMG on follow-up, (iii) breasts of women with family history of breast cancer with normal MMG on screening, (iv) breasts of women with normal first-time MMG, (v) a palpable lump in women less than 35 years-old, (vi) clinically suspected breast abscess.

The study was conducted to determine the comparative accuracy of USG and MMG in breast imaging at our centre and whether this was affected by patient's age and breast density. This study also aimed to determine if USG had detected breast cancers that were occult on MMG.

METHODS

This study was approved by the hospital technical and ethical committee. Patient informed consent was not required as this was a retrospective study.

SUBJECTS

This study involved patients who had breast imaging and biopsy at a tertiary hospital during an 18-month period. Details of patients (name, registration number, race, age and indication for imaging) who underwent breast biopsy were obtained from the department biopsy record books and imaging request forms. Details of breast imaging findings

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and histology of lesions biopsied were obtained from the hospital Integrated Radiology Information System (IRIS).

The USG and MMG findings were reported on a categorical scale of 1-5 according to level of suspicion for malignancy (1: no abnormality; 2: benign finding; 3: indeterminate finding; 4: suspicious lesion; 5: malignant lesion).

Dense breast was defined as 50% and more of the breast comprised of dense fibroglandular tissue on MMG.

USG Assessment
The USG assessment was with the Siemens Acuson S2000 (Germany) diagnostic unit using a 7.5 MHz transducer. Patients were examined in a supine position and turned slightly to the contralateral side with the ipsilateral upper limb extended cephalad. This position flattened the breast symmetrically over the chest wall. The breasts were scanned in longitudinal, transverse and radial planes.

Indications for breast USG included: to characterise a nodule detected on MMG, to assess breasts that were dense on MMG, to assess a palpable mass in patients aged less than 35 years, normal follow-up MMG in patients with previous history of breast cancer, normal 1st MMG, and in clinically suspected breast abscess. Characteristics of a breast nodule assessed on USG included: margins, internal echoes, posterior echoes, depth-width ratio and compressibility. Nodules were assigned a category according to level of suspicion for malignancy.

The USG were performed by the radiologist-in-training. The images were then reviewed by the radiologist as a 2nd reader. USG was repeated when there were discordant findings.

MMG Assessment
Two-view (cranial-caudal and medial-lateral oblique) MMG examinations were performed using the Hologic Lorad Selenia (United States) unit. Indications for MMG include: breast symptoms, previous breast cancer, hormone replacement therapy, and request for screening.

Characteristics of a breast nodule assessed on MMG included: shape, margin, density, presence of calcifications, architectural distortion, number of lesions, site of lesions and lymph nodes. Characteristics of microcalcifications assessed on MMG included: size, number, shape, margins, density, and distribution. Lesions were assigned a category according to level of suspicion for malignancy.

The MMG were evaluated by the radiologist-in-training who also decided on the need for USG. The images were then reviewed by the radiologist as a 2nd reader.

Statistical analysis
Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of USG and MMG were calculated with histology as the Gold Standard. For this purpose category 2 and 3 lesions were classified as benign and category 4 and 5 as malignant. In order to determine the significance in the differences in sensitivity and specificity between USG and MMG, statistical evaluation was performed using McNemar test with Yates Correction for lesions imaged with both modalities on the same day. The covariates were age group and breast density. Confidence interval was determined. Any difference was considered statistically significant when the p value was less than 0.05.

RESULTS

There were a total of 326 breast lesions (30 clustered microcalcifications, 296 nodules). When a patient had more than one lesion biopsied, data for demography and indications for imaging were entered for each lesion. The majority of malignant lesions were detected in Malays (60%) and in women aged 50 to 59 years (38%) (Table I). Of the 158 lesions where the indication for imaging could be obtained from the request form, about 40% had breast symptoms, about 20% had previous breast cancer; and another 40% were asymptomatic and were imaged because they were either on hormone replacement therapy (HRT) or had requested for screening (Table I).

Of the 326 lesions, 150 had USG only, 15 had MMG only and 161 had both performed on the same day. Lesions that were imaged with USG only were most frequently encountered in women aged less than 40 years, while lesions that were imaged with either MMG only or with both modalities were most frequently encountered in women aged between 50 to 59 years (Table II).

Lesions classified as Category 3, 4 and 5 on either one or both modalities had percutaneous biopsy. Lesions classified as Category 2 on either one or both modalities had percutaneous biopsy when the lesions were palpable or when risk factors were present. Histology showed 252 (77%) benign and 74 (23%) malignant lesions. Benign histology included: benign breast tissue (n=81), benign proliferative disease (n=74), fibroadenoma (n=61), mastitis or inflammation (n=21), papilloma (n=14), and phyllodes tumour (n=1). Malignant histology included: infiltrating ductal carcinoma (n=60), ductal carcinoma in situ (n=12), infiltrating lobular carcinoma (n=1), and lobular carcinoma in situ (n=1).

Compared with histology as the gold standard, USG had better sensitivity than MMG (82% and 49% respectively) (Table III and IV). The false negative rates for MMG and USG were 51% and 18% respectively (Table III).

In patients with normal MMG (Category 1), 7 had malignant lesions that were detected on USG (Table V). In patients with normal USG (Category 1), one had a malignant lesion detected on MMG (Table V). The 7 (20%) malignant lesions that were occult on MMG were nodules detected on USG and the one malignant lesion that was occult on USG was clustered microcalcifications detected on MMG.

To determine the significance of these observations using the McNemar test, only lesions which were imaged with both modalities on the same day (Table II) were compared and analysed. This comprised 161 lesions (3 clustered microcalcifications, 158 nodules) from a total of 326. The sensitivity and specificity of USG and MMG of these 161 lesions (Table VI) were compared and analysed.

Table I: Demographic details and indications for imaging according to breast cancer status

Demography, Indications for imaging	No. of Women with BenignBreast Lesions (%)	No. of Women with Breast Carcinoma (%)	No. of Women (% of Total)
Race			
Malay	149 (59)	45 (60)	194 (59)
Chinese	88 (35)	25 (34)	113 (35)
Indian	13 (5)	2 (3)	15 (5)
Others	2 (1)	2 (3)	4 (1)
Total	252 (100)	74 (100)	326 (100)
Age			
< 40	63 (25)	4 (6)	67 (20)
40 – 49	73 (29)	21 (28)	94 (29)
50 – 59	76 (30)	28 (38)	104 (32)
≥ 60	40 (16)	21 (28)	61 (19)
Total	252 (100)	74 (100)	326 (100)
Indications for imaging			
On HRT	33 (26)	3 (10)	36 (23)
Breast Screening	21 (16)	4 (13)	25 (16)
Breast Symptoms	54 (42)	16 (54)	70 (44)
Previous Breast Cancer	20 (16)	7 (23)	27 (17)
Total	128 (100)	30 (100)	158 (100)

Table II: Relationship between imaging investigations and age groups

Age Group	USG only		MMG only		USG and MMG		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
< 40	54	(36)	2	(13)	11	(7)	67	(20)
40 – 49	43	(29)	4	(27)	47	(29)	94	(29)
50 – 59	36	(24)	8	(53)	60	(37)	104	(32)
≥ 60	17	(11)	1	(7)	43	(27)	61	(19)
Total	150	(100)	15	(100)	161	(100)	326	(100)

Table III: MMG and USG results compared with histology results in all lesions imaged (n=326).

	Histology		Total (%)
	Benign (%)	Malignant (%)	
MMG			
Benign (%)	126 (72)	18 (10)	144 (82)
Malignant (%)	15 (8)	17 (10)	32 (18)
Total (%)	141 (80)	35 (20)	176 (100)
USG			
Benign (%)	202 (65)	13 (4)	215 (69)
Malignant (%)	38 (12)	58 (19)	96 (31)
Total (%)	240 (77)	71 (23)	311 (100)

Table IV: Validity of USG and MMG in all lesions imaged (n=326)

Validity	USG	MMG
Sensitivity (%)	82	49
Specificity (%)	84	89
PPV (%)	60	53
NPV (%)	94	88
Accuracy (%)	84	81

Table V: Categorical score of MMG and USG in comparison to histology

Categorical scale	No. of Women with Benign Breast Lesions (%)	No. of Women with Breast Carcinoma (%)	No. of Women (% of Total)
MMG Scoring			
1	33 (23.40)	7 (20.00)	40 (22.73)
2	62 (43.97)	5 (14.29)	67 (38.07)
3	31 (21.99)	6 (17.14)	37 (21.02)
4	14 (9.93)	13 (37.14)	27 (15.34)
5	1 (0.71)	4 (11.43)	5 (2.84)
Total	141 (100.00)	35 (100.00)	176 (100.00)
USG Scoring			
1	1 (0.42)	1 (1.41)	2 (0.64)
2	90 (37.50)	2 (2.82)	92 (29.58)
3	111 (46.25)	10 (14.08)	121 (38.92)
4	37 (15.41)	43 (60.56)	80 (25.72)
5	1 (0.42)	15 (21.13)	16 (5.14)
Total	240 (100.00)	71 (100.00)	311 (100.00)

Table VI: MMG and USG results compared with histology in lesions imaged with both modalities (n=161)

	Histology		Total (%)
	Benign (%)	Malignant (%)	
MMG			
Benign (%)	117 (73)	18 (11)	135 (84)
Malignant (%)	12 (7)	14 (9)	26 (161)
Total (%)	129 (80	32 (20)	161 (100)
USG			
Benign (%)	102 (63)	8 (5)	110 (68)
Malignant (%)	27 (17)	24 (15)	51 (32)
Total (%)	129 (80)	32 (20)	161 (100)

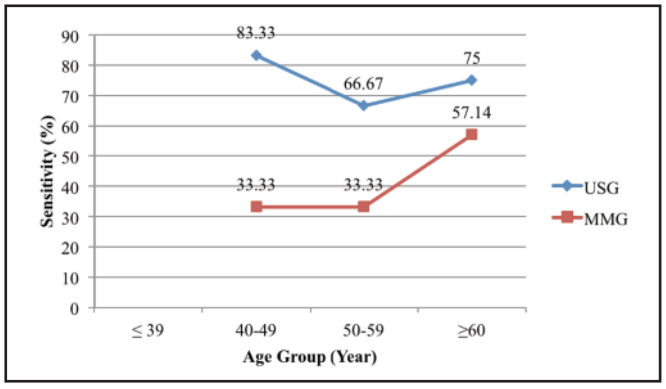

Fig. 1 : Graph of sensitivity of USG and MMG in different age groups.

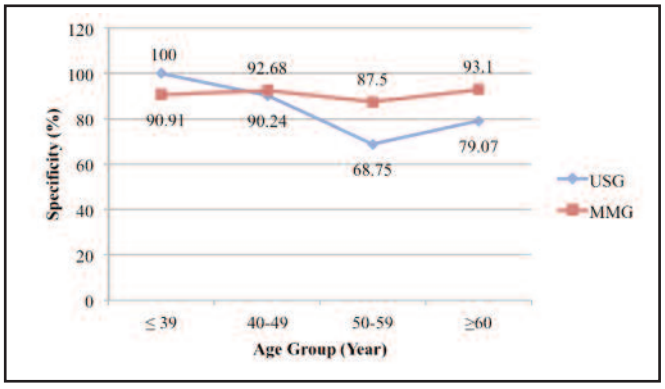

Fig. 2 : Graph of specificity of USG and MMG in different age groups.

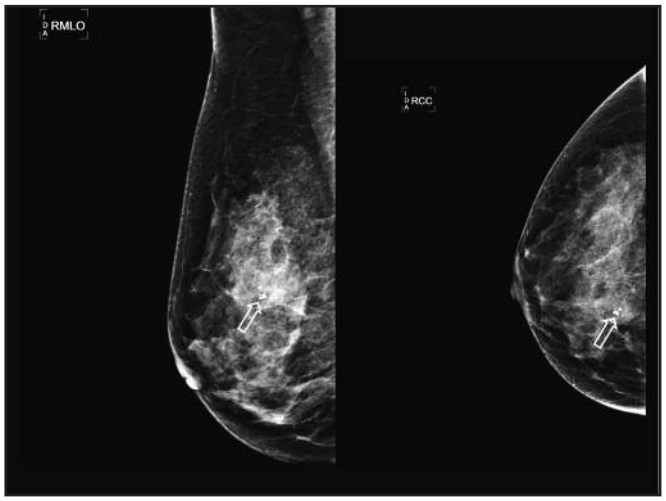

Fig. 3 : Right mammogram of a 58-year-old woman. The breasts were dense. Coarse calcifications were noted at the right upper-mid quadrant (block arrow) and reported as involuting fibroadenoma (Category 2). There was no nodule seen.

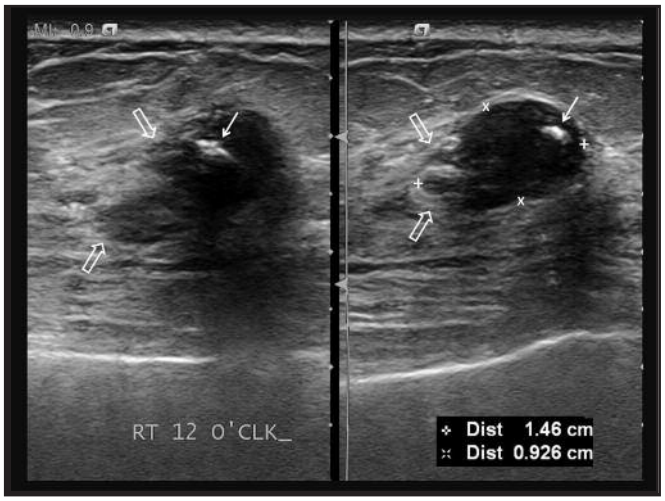

Fig. 4 : The ultrasound of the breast of the same patient as in Fig. 3. The calcifications seen in the mammogram were noted to be within a hypoechoic nodule (arrow). This nodule was reported to be suspicious of malignancy (Category 4) because its lateral margins were irregular (block arrows). Percutaneous biopsy with ultrasound guidance revealed benign breast tissue.

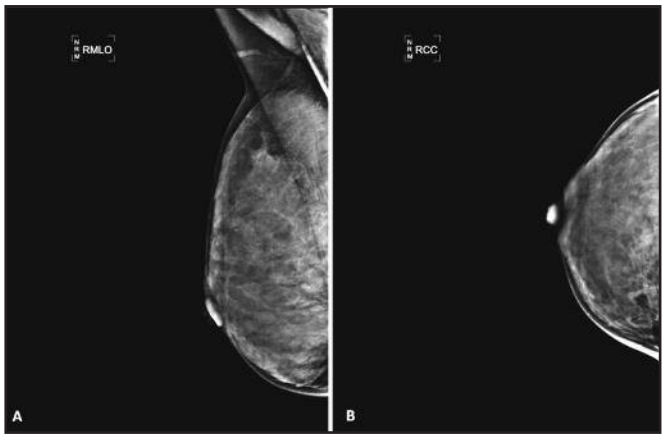

Fig. 5 : (A) Mediolateral and (B) craniocaudal mammogram views of the right breast. The breast was very dense and no dominant mass was detected.

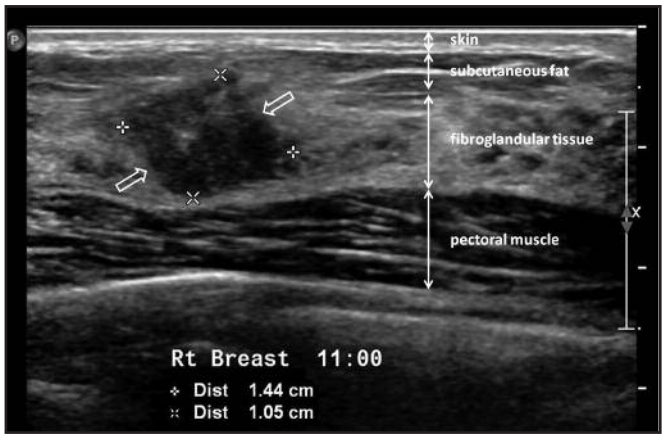

Fig. 6 : Ultrasound of the breast of the same patient as in Fig. 5 revealed an irregular, inhomogenous, hypoechoic nodule (block arrows). Percutaneous biopsy with ultrasound guidance revealed infiltrating ductal carcinoma. Notice that the ultrasound image clearly showed the different layers of breast tissue.

The 75% sensitivity of USG was 31% (95% CI 15% to 47%) higher than the 44% sensitivity of MMG. The higher sensitivity of USG was statistically significant (X^2_1=6.095, p=0.014).

The 91% specificity of MMG was 12% (95% CI 5% to 18%) higher than the 79% specificity of USG. The higher specificity of MMG was statistically significant (X^2_1=27.114, p<0.001).

Of the 32 lesions with malignant histology, 6 were in women aged less than 50 years. Of the 129 lesions with benign histology, 52 were in women aged less than 50 years.

In women aged less than 50 years, the sensitivity of USG was 50% (95% CI 10%-90%) higher than the sensitivity of MMG (Fig. 1). However, due to the small number of total lesions with malignant histology (n=6), there was no statistically significance difference in sensitivity for the two modalities (X^2_1=0.000, p=1.000). In women aged 50 years and above, the sensitivity of USG was 27% (95% CI 19%-36%) higher than the sensitivity of MMG. The higher sensitivity of USG was statistically significant (X^2_1=5.866, p=0.015).

On the other hand, in women aged less than 50 years, the specificity of USG and MMG were the same (Fig. 2). In women aged 50 years and above, the specificity of MMG was 21% (95% CI 12%-31%) higher than specificity of USG. The higher specificity of MMG was statistically significant (X^2_1=11.251, p=0.001).

In general, USG was more sensitive than MMG in both age groups. But MMG was more specific in the older age group.

Of the 32 lesions with malignant histology, 10 were in women with dense breasts. Of the 129 lesions with benign histology, 69 were in women with dense breasts.

In women with dense breasts, the sensitivity of USG was 40% (95% CI 10%-70%) higher than the sensitivity of MMG. However, due to the small number of total lesions with malignant histology (n=10), there was no statistically significant difference in sensitivity for the two modalities (X^2_1=0.234, p=0.628). In women with non-dense breasts, the sensitivity of USG was 27% (95% CI 9%-46%) higher than the sensitivity of MMG. The higher sensitivity of USG was statistically significant (X^2_1=4.585, p=0.032).

On the other hand, in women with dense breasts, the specificity of MMG was 13% (95% CI 5%-21%) higher than the specificity of USG. The higher specificity of MMG was statistically significantly (X^2_1=18.887, p<0.001). In women with non-dense breasts, the specificity of MMG was 10% (95% CI 0.02%-20%) higher than specificity of USG. The higher specificity of MMG was statistically significant (X^2_1=6.123, p=0.013).

In general, USG was more sensitive than MMG in women regardless of breast density. But MMG was more specific in both dense and non-dense breasts.

DISCUSSION

In this study, the accuracy for the detection of breast cancer was 84% with USG and 81% with MMG. Sensitivity for this study was higher with USG (82%) compared with MMG (49%). These findings are similar to previous studies that showed a higher sensitivity for USG (73-83%) as compared with MMG (52-78%) [5-8].

The higher sensitivity of USG was noted in studies that involved either women with breast symptoms or asymptomatic women in a screening program [5-8]. This study population comprised a combination of both symptomatic and asymptomatic women. This is because this study is not based in a breast screening centre but in a general radiology department where there is no formal breast screening program. Where information regarding indication for imaging was available, slightly more women were asymptomatic (including those with past history of breast cancer) compared with symptomatic women. In this study, as in previous studies, USG was performed with knowledge of clinical data and MMG findings. Although this is the logical clinical sequence of investigations, the USG operator may have been influenced by this information. The knowledge of MMG findings creates bias in favour of USG [9]. For example, when an abnormality has been detected on MMG, the subsequent USG would of course be targeted to that abnormality and USG would appear to be at least as sensitive as MMG. When MMG-negative cases proceed to USG, for example in patients with dense breasts, USG could appear more sensitive than MMG but the false negative of USG would not be recognised.

Many reports have concluded that USG is more sensitive in young women and those with dense breasts and that the sensitivity of MMG improves with age when the breasts involute and become fatty [10-13]. This study did not concur with these reports because USG was found to be more sensitive regardless of age. However, MMG did show better specificity in those older than 50 years. Furthermore, this study showed that USG was more sensitive while MMG more specific regardless of the breast density. Although these findings differ from previous reports, the conclusion that USG is an effective supplement to MMG remains. The combination of USG and MMG has been shown to have higher sensitivity in detecting breast cancer in symptomatic patients of all ages [14,15] as well as in the asymptomatic screening population [6, 8].

The observed higher false positive rate of USG as compared to MMG (Tables III and VI, Figs. 3 and 4) had also been noted in previous reports [16-18]. This higher false positive rate of USG resulted in comparatively higher specificity of MMG (Table IV, Fig. 2).

It has been reported that cancers that are occult on MMG can be detected by USG in 10-40% of cases depending on the patient's age and breast density [6, 19]. In this study, 20% of breast cancers detected were occult on MMG and seen only on USG. Dense breasts obscure lesions within the breasts. MMG can demonstrate the entire breasts in 4 views (bilateral craniocaudal and bilateral mediolateral oblique views). However, MMG produces 2-dimensional images of 3-dimensional organs. As such, there is considerable overlap of breast structures. It is easy to overlook lesions when the breasts have a lot of fibroglandular tissue and are dense on MMG (Fig. 5). Like normal fibroglandular tissue, malignant lesions are also dense on MMG. Conversely, USG images of the breasts show structures of the breasts from skin to chest wall without overlap of structures (Fig. 6). Malignant lesions are hypoechoic on USG in contrast to the relatively hyperechoic normal breast tissue. As such, USG imaging is not impaired by dense breast parenchyma. The downside of USG is that multiple images have to be viewed on real-time scanning in order to view the entire breasts, unlike MMG where just 4 images can demonstrate the entire breasts.

The ability of USG to show images of the breasts without overlap of structures has lead to additional MMG views (such as lateromedial, mediolateral, craniocaudal with medial or lateral bias, roll, Cleopatra and cleavage views) to become obsolete. Additional views (such as coned compression) to study the margins of detected nodules and to determine if there is a lesion in the presence of asymmetry of breast density are often replaced by USG which does not use ionising radiation and does not cause patient pain and discomfort. Much has been said about USG being operator dependent. However, USG technology has improved tremendously over the years. Machines are now very user-friendly and have programmed settings for specific organs or body parts. In most radiology centres, radiologists who are involved in breast imaging are competent in reading MMG images as well as in performing USG. Furthermore, USG provides convenient and easy guidance for percutaneous procedures such as biopsy of a breast lesion.

Breast density is the main predictor of mammography sensitivity [11-13, 15]. Apart from USG, MRI has been used to supplement MMG of dense breasts [20-22]. However, MRI is expensive and not easily available. Not all imaging centres with MRI have the software and hardware for breast imaging and MRI-guided biopsy. Furthermore, it is an invasive procedure as imaging requires intravenous contrast.

Our results indicate that USG is a more accurate modality for detecting breast cancers that appear as nodules. Despite all the advantages of USG, it cannot replace MMG as it can still miss cancers that a MMG would detect. In this study, USG missed a cancer that presented as a cluster of microcalcifications on MMG.

CONCLUSION

Accuracy of USG was higher compared with MMG. USG was more sensitive than MMG regardless of age group. But MMG was more specific in those aged 50 years and older. USG was more sensitive and MMG was more specific regardless of breast density. In this study, 20% of breast cancers detected were occult on MMG and seen only on USG.

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