AGREEMENT BETWEEN HANDHELD ULTRASOUND AND AUTOMATED BREAST VOLUME SCANNER IN DETECTING CHARACTERISTIC OF COMPLEX BREAST CYSTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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LISTS OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

AP	Anteroposterior
ABVS	Automated breast volume scanner
HHUS	Handheld Ultrasound
HUSM	Hospital University Sains Malaysia
PACS	Picture Archiving and Communication System
SD	Standard Deviation
W	Width
BI-RADS	Breast imaging Reporting and Data System
ACR	American College of Radiology
sUSBA	Syngo Ultrasound Breast Analysis (sUSBA)
MPR	Multiplanar Reformation
MRI	Magnetic Resonance Imaging

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ABSTRAK

Latar belakang: Kantung air payudara dikelaskan sebagai kantung air payudara yang ringkas, rumit, dan kompleks. Kantung air payudara kompleks dikelaskan sebagai BI-RADS 4 kerana terdapat 23 hingga 31% kemungkinan mengubah kepada kanser. Ultrasound payudara dianggap sebagai pemeriksaan yang lazim digunakan dalam pengesanan dan pencirian ketumbuhan payudara. Memandangkan beberapa kelemahan dalam ultrasound konvensional, pengimbas volumetrik payudara automatik telah diperkenalkan untuk mengatasi kelemahan ultrasound konvensional. Tujuan kajian ini tertumpu kepada persetujuan antara ultrasound konvensional dan pengimbas volumetrik payudara automatik dalam pengesanan ciri-ciri kantung air payudara yang kompleks termasuk septa tebal, dinding tebal and komponen tisu.

Metodologi: Kajian ini dijalankan di Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan dari 3 Oktober 2021 sampai 2 Oktober 2023. Data dikumpul secara retrospektif dan prospektif. Secara retrospektif, data dikumpul daripada kumpulan pesakit dengan kantung air payudara kompleks yang telah menjalani pengimbas volumetrik payudara automatik dan ultrasound konvensional di Jabatan Radiologi HUSM daripada sistem imej jabatan radiology. Secara prospektif, pesakit yang didapati mempunyai kantung air payudara kompleks dalam ultrasound konvensional, persetujuan akan diambil daripada pesakit dan pengimbas volumetrik payudara automatik akan dijalankan pada pesakit. Untuk semua objektif, persetujuan antara ultrasound konvensional dan pengimbas volumetrik payudara automatik akan dianggarkan menggunakan statistik Kappa. Statistik Kappa ialah ukuran persetujuan antara dua penilai. Anggaran Kappa akan dibentangkan sebagai nilai Kappa, disertai dengan konfidensial selang 95%. Nilai Kappa < 0 sebagai menunjukkan persetujuan yang sangat lemah dan 0.01–0.20 sebagai lemah, 0.21–0.40 sebagai sederhana lemah, 0.41– 0.60 sebagai sederhana, 0.61–0.80 sebagai baik, dan 0.81–1.00 sebagai persetujuan hampir sempurna.

Keputusan: Purata umur keseluruhan (SD) bagi pesakit adalah 45.9 (9.4) tahun. 40 pesakit dan 61 kantung air payudara termasuk dalam kajian ini. Saiz purata kantung air payudara berukuran 0.6cm dalam diameter anterior - posterior dan 1.1cm dalam kelebaran. Terdapat persetujuan yang baik antara ultrasound kenvensional dan pengimbas volumetrik payudara automatik dalam pengesanan septa tebal dan komponen tisu yang menunjukkan persetujuan kappa 0.701 (95% KI : 0.525, 0.877) and 0.758 (95% KI :0.589,0.927). Terdapat persetujuan yang hampir sempurna antara ultrasound konvensional dan pengimbas volumetrik payudara automatik dalam pengesanan dinding tebal yang menunjukkan persetujuan kappa sebanyak 0.880 (95% KI : 0.649, 1.0).

Kesimpulan: Oleh sebab terdapat persetujuan yang baik antara HHUS dan ABVS dalam pengesanan ciri-ciri kantung air payudara kompleks, HHUS boleh dikecualikan dalam pencirian lebih lanjutan untuk kantung air payudara kompleks. Oleh itu, masa pengimbasan dapat dikurangkan. Walau bagaimanapun, kohort yang lebih besar dengan lebih banyak bilangan kantung air payudara kompleks diperlukan untuk mendapat keputusan yang lebih tepat.

Kata Kunci: kantung air payudara kompleks, pengimbas volumetrik payudara automatik, ultrasound kenvensional

ABSTRACT

Background: Breast cysts are generally categorized as simple, complicated and complex breast cyst. Complex cystic breast lesions are classified as BI-RADS 4 as there are 23 to 31 % of chance being malignant. Breast ultrasonography is the first-line examination in detection and characterization of breast lesions. In view of few limitations of handheld ultrasound (HHUS), automated breast volume scanner (ABVS) was introduced to overcome the limitation. The purpose of this study is to focus on agreement between HHUS and ABVS in detecting characteristic of complex breast cysts which are thick septa, thick wall and solid component as there is no similar study are done before.

Methods: A cross-sectional study was conducted in Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan from 3rd October 2021 to 2nd October 2023. Data was collected retrospectively and prospectively. Retrospectively, the data was taken from pool of patients with complex breast cysts who underwent ABVS and HHUS in Radiology Department HUSM from Picture Archiving and Communication System (PACS). Prospectively, complementary ABVS was performed in patients who had complex breast cyst after performed HHUS by radiology medical officers with at least 2 years of experience in radiology service after obtaining patient consent. Agreement between HHUS and ABVS was estimated using Kappa statistic (unweighted Kappa). Kappa statistics is a measurement of the agreement between two raters. The estimated Kappa was presented as the Kappa value, accompanied by its 95% confidence interval. Kappa value < 0 as indicating poor agreement and 0.01–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.

Results: The overall mean (SD) age for the patient was 45.9 (9.4) years old. Total 40 patients with 61 breast lesions were included in this study. The average size of the lesion was 0.6cm in anterior-posterior diameter and 1.1cm in width. There was substantial agreement between HHUS and ABVS in detecting thick septa and solid component which showed kappa agreement of 0.701 (95% CI: 0.525, 0.877) and 0.758 (95% CI :0.589,0.927) respectively. There was almost perfect agreement between HHUS and ABVS in detecting thick wall which showed kappa agreement of 0.880 (95% CI: 0.649, 1.0).

Conclusion: Since there is good agreement between HHUS and ABVS in detecting features of complex breast cysts, complimentary HHUS can be exempted in further characterization of the complex breast cyst. Thus, it may help in reducing scanning time. However, larger cohort with more numbers of complex breast cysts is needed to yield favourable results.

Keyword: Complex breast cyst, automated breast volume scanner, handheld ultrasound

CHAPTER 1: BACKGROUND

1.1 Introduction

Breast cysts are generally categorized as simple, complicated, or complex cysts as their management differ for each type. Simple cysts are described as well circumscribed anechoic, round, or oval shape lesions with imperceptible wall and increased through transmission of sound waves. Complicated breast cysts have characteristic of simple breast cysts but contain internal echoes or debris that may change with patient position. Complex breast cysts are described as cysts with thick walls, thick septa, intracystic masses, or other discrete solid components(Doshi et al., 2007).

American College of Radiology (ACR) has created a standardized system of reporting breast pathology on mammography, ultrasound and magnetic resonance imaging - Breast Imaging Reporting and Data System (BI-RADS) which encourages consistency between reports and allows better communication between radiologists and physicians(Spak et al., 2017). Simple breast cysts are considered benign and classified as BI-RADS 2 as there are no further intervention required. Complicated cysts are classified as BI-RADS 3 which require short term imaging follow up as there are less than 2 % risk of malignancy. Complex cystic breast lesions are classified as BI-RADS 4 as there are 23 to 31 % of chance being malignant. Thus, percutaneous or surgical biopsy is usually indicated (Doshi et al., 2007).

Breast ultrasonography is considered the first-line examination in detection and characterization of breast lesions. However, there are a few limitations for handheld ultrasound (HHUS) such as time consuming, high number false positive, lack of standardized technique, operator dependence, non-reproducible and must be conducted by a sonographer or physician with the knowledge of ultrasound physics and anatomy. More than a decade ago, automated breast volume scanner (ABVS) was introduced which is an option to overcome limitation of HHUS. Among the advantages of ABVS include consistency and reproducibility, not operator dependent, less time consuming, and consistent image acquisition time. The average image acquisition time is 15 minutes for a patient for standard three views and anyone can be trained to operate the ABVS. Besides, ABVS has additional diagnostic value as the coronal view is unique and allow detection of retraction phenomenon which is specific for breast malignancy (Shin et al., 2015).

1.2 Objective

1.2.1 General Objective

To assess the agreement between HHUS and ABVS in detecting characteristic of complex breast cyst.

1.2.2 Specific Objective

1. To determine the level of agreement between HHUS and ABVS in detecting thick wall.
2. To determine the level of agreement between HHUS and ABVS in detecting thick septa.
3. To determine the level of agreement between HHUS and ABVS in detecting solid component.

1.3 Hypothesis

There is an agreement between HHUS and ABVS in detecting characteristic of complex breast cyst.

1.4 Research question

1. What is the agreement between HHUS and ABVS in detecting thick wall?
2. What is the agreement between HHUS and ABVS in detecting thick septa?
3. What is the agreement between HHUS and ABVS in detecting solid component?

CHAPTER 2: LITERATURE REVIEW

2.1 Breast Cyst

According to American Journal of Roentgenology, breast cysts can be classified into three categories which are simple, complicated and complex breast cysts. The characteristics of simple cyst include anechoic, well circumscribed with thin echogenic wall, increased through-transmission, and thin edge shadow. Simple cysts are classified as BI-RADS 2. The possible differential diagnosis for simple breast cysts includes hematoma, galactocele, and oil cyst (Hines et al., 2010). Complicated cysts are cysts that contains internal echoes or fluid debris level. The possible differential diagnosis for a complicated cyst is similar to a simple cyst with the addition of abscess (Hines et al., 2010). Isolated complicated cyst is classified as BI-RADS 3 as there is less than 2 % chance of malignancy. Short-interval ultrasound follow-up (six month) and then periodic sonographic surveillance should be suggested (Sickles et al., 2013).

Characteristic of complex breast cyst includes thick walls or some discrete solid component, such as mural nodule or septa with thickness more than 0.5 mm (Hines et al., 2010). There are wide range of differential diagnosis for complex breast cysts which include benign and malignant condition. The benign condition includes inflammatory cyst, fat necrosis, papilloma, and fibrocystic mastopathy. The malignant condition includes encapsulated intracystic papillary carcinoma, solid papillary carcinoma, and invasive intraductal carcinoma. Complex breast cysts have malignancy rate varying from 23% to 31%. Thus, is it classified at least as BI-RADS 4 and requiring percutaneous biopsy for histopathology correlation (Athanasiou et al., 2014).

2.2 BI-RADS

A classification system for breast imaging includes mammography, ultrasound and magnetic resonance imaging (MRI) of the breast has been proposed by American College of Radiology (ACR). It is called Breast imaging Reporting and Data System (BI-RADS). The purpose of BI-RADS is to provide standardized breast imaging terminology, assessment structure and organization of radiology report. Thus, radiologists able to communicate the result with the referring physician clearly through BI-RADS reporting with final assessment and management recommendation (Sickles et al., 2013). In BI-RADS lexicon for ultrasound, the background echo pattern of breast can be described as homogeneously fatty, homogeneously fibroglandular or heterogeneous. This background breast tissue composition can influence sensitivity of lesion detection. For example homogeneous fibrofatty breast generate weak contrast thus reduce sensitivity while heterogeneous breast background echotexture cause false positive (Levy et al., 2007).

There are several characters should be documented when describing a mass. These characters include shape, orientation, margin, boundary of the lesion, type of echogenicity, posterior acoustic features and effect on surrounding tissues. Besides, other abnormalities like presence of calcification or vascularity, foreign body, intramammary and axillary nodes should be included in the report (Levy et al., 2007). Correlation should be done for breast ultrasound with physical finding, mammography, MRI or other modalities and the report should include other types of examination that are performed on the same day. Besides, the report should provide the overall assessment using BI-RADS ultrasound categories one to six and management recommendation (Sickles et al., 2013). Each BI-

RADS category has recommended management and risk of malignancy as described in Figure 1.

Assessment	Management	Likelihood of Cancer
Category 0: Incomplete — Need Additional Imaging Evaluation	Recall for additional imaging	N/A
Category 1: Negative	Routine screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine screening	Essentially 0% likelihood of malignancy
Category 3: Probably Benign	Short-interval (6-month) follow-up or continued surveillance	> 0% but ≤ 2% likelihood of malignancy
Category 4: Suspicious	Tissue diagnosis	> 2% but < 95% likelihood of malignancy
Category 4A: *Low suspicion* for malignancy		> 2% to ≤ 10% likelihood of malignancy
Category 4B: *Moderate suspicion* for malignancy		> 10% to ≤ 50% likelihood of malignancy
Category 4C: *High suspicion* for malignancy		> 50% to < 95% likelihood of malignancy
Category 5: Highly Suggestive of Malignancy	Tissue diagnosis	≥ 95% likelihood of malignancy
Category 6: Known Biopsy-Proven Malignancy	Surgical excision when clinically appropriate	N/A

Figure 1: Table shows concordance between BI-RADS assessment categories and management recommendations (Adapted from ACR BI-RADS Atlas 5th Edition 2013)

2.3 Handheld Ultrasound for Breast

Ultrasound images able to demonstrate different soft tissue layers within the breast. The skin appears as bright line as it is highly reflective. Fatty tissue appears dark as it causes lower echoes. Parenchymal and fibrous tissue appears bright as it reflects ultrasound echoes strongly. Cooper's ligaments and supporting glandular structures of the breasts are also appears as thin echogenic fibres in ultrasound images. Breast lesions generally appear hypoechoic than surrounding tissues (Chandra M. Sehgal et al., 2006).

Among the main application for breast ultrasound includes for differentiation between solid and cystic lesions, to evaluate palpable masses which are not visualized or obscured by dense breast in mammography, for evaluation of palpable masses in young and pregnant lady, determine lymph node status, act as screening tool for detection of occult breast cancer in dense breast, and provision of imaging guidance for biopsy and localization (Kyu et al., 2005)(Chandra M. Sehgal et al., 2006).

The accuracy of ultrasound in detecting breast cyst has been reported to be almost 100% and sonographic criteria of simple cyst can be easily differentiate from complex breast cyst (Article, 2008). There are four categories of complex breast cysts depend on morphology which includes cysts with a thick wall (≥ 0.5 mm), cysts with thick internal septa (≥ 0.5 mm), predominantly cystic complex masses (more than 50% cystic component) and predominantly solid complex masses (more than 50% solid components) including peripheral cystic components (Athanasiou et al., 2014).

Besides, colour and power Doppler imaging can be used in differentiate benign and malignant lesions. The Sehgal et al. study measures vascularity of breast masses quantitatively using Doppler sonographic imaging and differentiate vascular pattern between benign and malignant lesion. The results suggest that visualization of blood vessels at the level of arterioles and venules is possible using colour Doppler and power Doppler imaging with modern ultrasound scanners. The results show that malignant masses have increased vascularity compared to benign lesion. The benign masses are about 2.29 times more vascular than the surrounding tissue while the malignant masses are about 5.01 times more vascular compared to surrounding tissue (C. M. Sehgal et al., 2000).

Another additional features of ultrasound for characterize breast mass is elastography. It is used to determine tumour elasticity in patient with breast cancer. Fibroadenoma are two times stiffer than normal breast tissue while breast cancer can be up to 15 times stiffer than surrounding breast parenchyma. The significant difference in elasticity of breast lesions could help in differentiation of malignant and benign lesion (Chandra M. Sehgal et al., 2006). Kolb et al study in 2002 shows that sensitivity of mammography in detecting breast cancer decrease with increasing breast density. The sensitivity of mammography in women with fatty breasts is 98 % and it declines to 48% in women with highest density category. Screening ultrasound in women in dense breasts shows increase in detection of occult cancer. 70% of cancers found only with screening ultrasound are subcentimer and 89% are node negative (Kolb et al., 2002). However, it is sometimes a challenging task to differentiate benign from malignant lesion. The accuracy of this modality highly depends on operator skills and experience (Kyu et al., 2005). Besides there are also another technical drawback such as it is not reproducible and time consuming.

2.4 Automated Volumetric Breast Scanner (ABVS)

Automated breast ultrasound is recently introduced to overcome limitation of traditional HHUS. There are several types of automated breast ultrasound system. The main categories include prone and supine scanner. The average examination time is approximately 15 minutes. The data is transferred to workstation and images are displayed in native axial plane and reformatted coronal and sagittal plane for further interpretation. This advantage of multiplanar reformation enable the images to be reviewed retrospectively. Furthermore, the coronal plane introduces a new diagnostic information i.e. the retraction phenomenon which has high diagnostic accuracy for breast malignancy (Zanotel et al., 2018).

Compared to HHUS, ABVS has a few advantages such as less operator dependent as ABVS is more consistent, increase reproducibility and less time consuming. Besides, anyone can be trained to operate ABVS equipment while HHUS needs to be conducted by radiologist or trained sonographer. Furthermore, its multiplanar reconstruction (MPR) has introduced new diagnostic information especially the coronal view. However, the main limitation of ABVS includes unable to assess vascularity and tissue elasticity of breast lesions as well as exclusion of axillary region from field of view (Zanotel et al., 2018).

Many studies were done to compare ABVS and HHUS in detection and characterization of breast lesions as well as evaluation of the diagnostic performance of ABVS. Figure 2 shows summary of results from few studies in comparing detection rate of breast lesions between ABVS and HHUS. Most of the authors reported that detection rate of the breast lesions is similar between ABVS and HHUS. However, there are some studies reported ABVS has higher detection rate HHUS. Zhang et al and Xiao et al studies demonstrated that ABVS can detect higher number of breast lesions compared to HHUS (Zanotel et al., 2018).

Study	Number (patients, lesions)	HHUS detection rate (%)	ABUS detection rate (%)	*p*
Wang et al. [23]	213, 239	98.7	99.6	n. s.
Xiao et al. [31]	300, 417	78.2	100	<0.001
Wang et al. [39]	155, 165	95.8	97.6	n. s.
Lin et al. [40]	81, 95	100	100	n. s.
Kim et al. [41]	38, 66	93.9	84.8, 84.8, 86.3[a]	n. s.
Zhang et al. [42]	81, 99	60.6, 85.8[b]	89.9, 100[b]	<0.05, n. s.[b]

n. s. not significant ($p > 0.05$)

[a] Results for three readers

[b] Results for two readers. The difference in the lesion detection was significant only for one of the two readers ($p = 0.0006$)

Figure 2: Table shows results of study comparing ABVS and HHUS in breast lesion detection rate (Adapted from Zanotel et al 2018)

Shin et al study was done to evaluate interobserver agreement on lesion detection and characterization in ABVS by five radiologists. It reported that the lesion detection rate is increasing as the size of the lesion increase. When the mean lesion diameter is greater than 1.2cm, the detection rate is around 92%. This study found moderate agreement on lesion boundary, echogenicity and posterior acoustic feature. Higher rate of agreement was found for malignant features compared to benign features. Higher rate of agreement also found for lesions with diameter greater than 0.7cm (Shin et al., 2011).

Another study by Wang et al in 2012 to assess the diagnostic value of conventional handheld HHUS and ABVS in differentiating benign and malignant breast lesions. In this study, the lesions are divided into four groups according to their size which is Group 1 (0–

0.9 cm), Group 2 (1–1.9 cm), Group 3 (2.0–2.9 cm), and Group 4 (>3 cm). The diagnostic accuracy, sensitivity, specificity, positive predictive value, negative predictive value, false positive rate, and false negative rate were calculated according to size of the masses in this study. Figure 3 shows the summary of the result of this study. It shows that when the masses were less than 1 cm in diameter, the sensitivity of ABVS was better than HHUS. The diagnostic accuracy of ABVS was similar to HHUS when masses were larger than 1 cm in diameter. The sensitivity of the ABVS and HHUS in detecting lesion more than 3 cm is same which is 93.1% (Wang et al., 2012).

Assessment of 239 breast masses with ABVS and HHUS.

Size	Method	SE	SP	AC	FPR	FNR	PPV	NPV
All lesions	ABVS	95.30%	80.50%	85.80%	19.50%	4.70%	73.00%	93.30%
	HHUS	90.60%	82.50%	85.30%	17.50%	9.40%	74.00%	94.10%
0–0.9 cm	ABVS	83.30%	66.70%	70.80%	33.30%	16.70%	83.30%	92.30%
	HHUS	50.00%	66.70%	62.50%	33.30%	50.00%	33.30%	80.00%
1–1.9 cm	ABVS	100%	85.90%	89.70%	14.10%	0%	72.70%	100%
	HHUS	95.80%	85.90%	88.60%	14.10%	4.20%	71.90%	98.20%
2.0–2.9 cm	ABVS	96.20%	81.60%	87.50%	18.40%	3.80%	78.10%	96.90%
	HHUS	92.30%	84.20%	87.50%	15.80%	7.70%	80.00%	94.10%
>3 cm	ABVS	93.10%	76.50%	84.10%	23.50%	6.90%	77.10%	92.90%
	HHUS	93.10%	82.40%	87.30%	17.60%	6.90%	81.80%	93.30%

SE, sensitivity; SP, specificity; AC, accuracy; FPR, false-positive rate; FNR, false-negative rate; PPV, positive predictive value; NPV, negative predictive value.

Figure 3: Table shows assessment of 239 breast masses with ABVS and HHUS (Adapted from (Wang et al., 2012)

Another study by Wang et al in 2016 on identifying ABVS features that distinguish benign from malignant lesions. Complex breast cysts were categorized into six categories and showed in Figure 4. Comparisons were done between the histopathology results and ABVS coronal plane features of the lesions and showed that ABVS can reveal sonographic features of the lesions along the coronal plane may offer better detection of malignant, predominantly cystic masses and provide high clinical values.

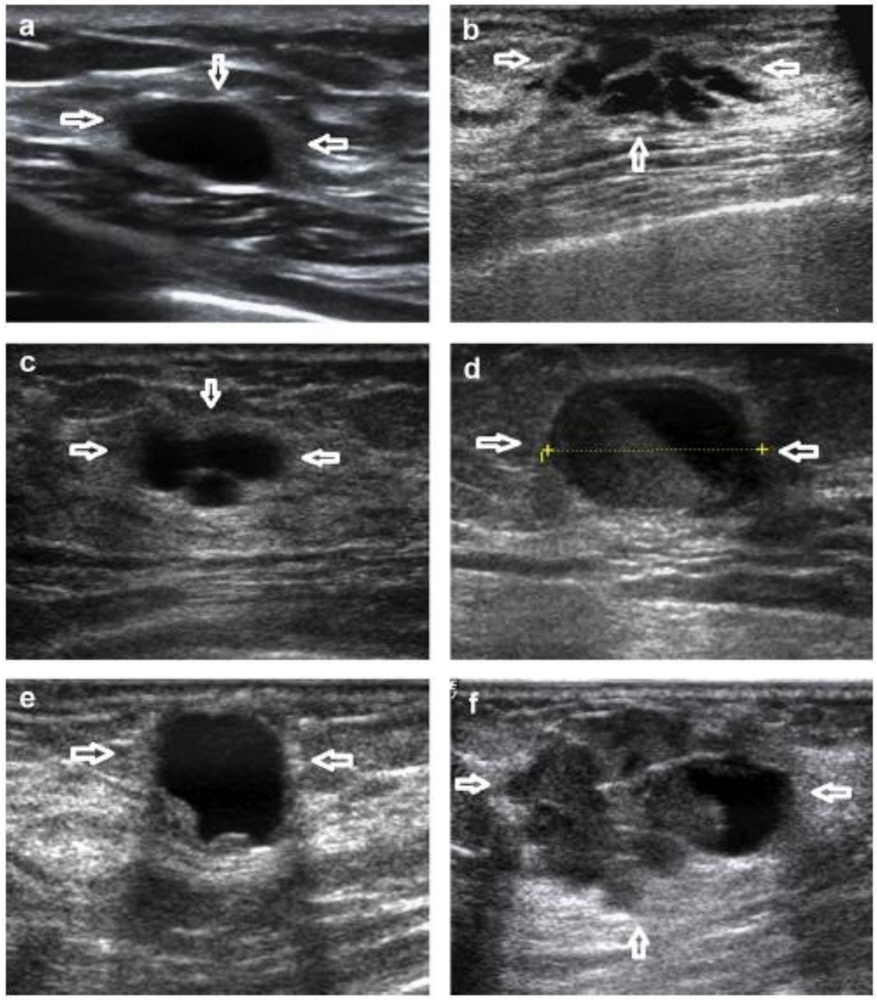

Figure 4: Figures shows categories of cystic breast lesions (arrows) based on automated breast volume scanning sonographic imaging. In this study, the breast cysts are categorized into 6 types.

(a) Type I - Simple breast cyst. (b) Type II - Clustered of simple breast cysts. (c) Type III - Cyst with thin septa. (d) Type IV - Cyst with internal echogenic debris. (e) Type V - Cystic mass with more than 50% cystic component. (f) Type VI - Cystic mass with less than 50% cystic component. (Adapted from Wang et al., 2016)

2.5 Conceptual Framework

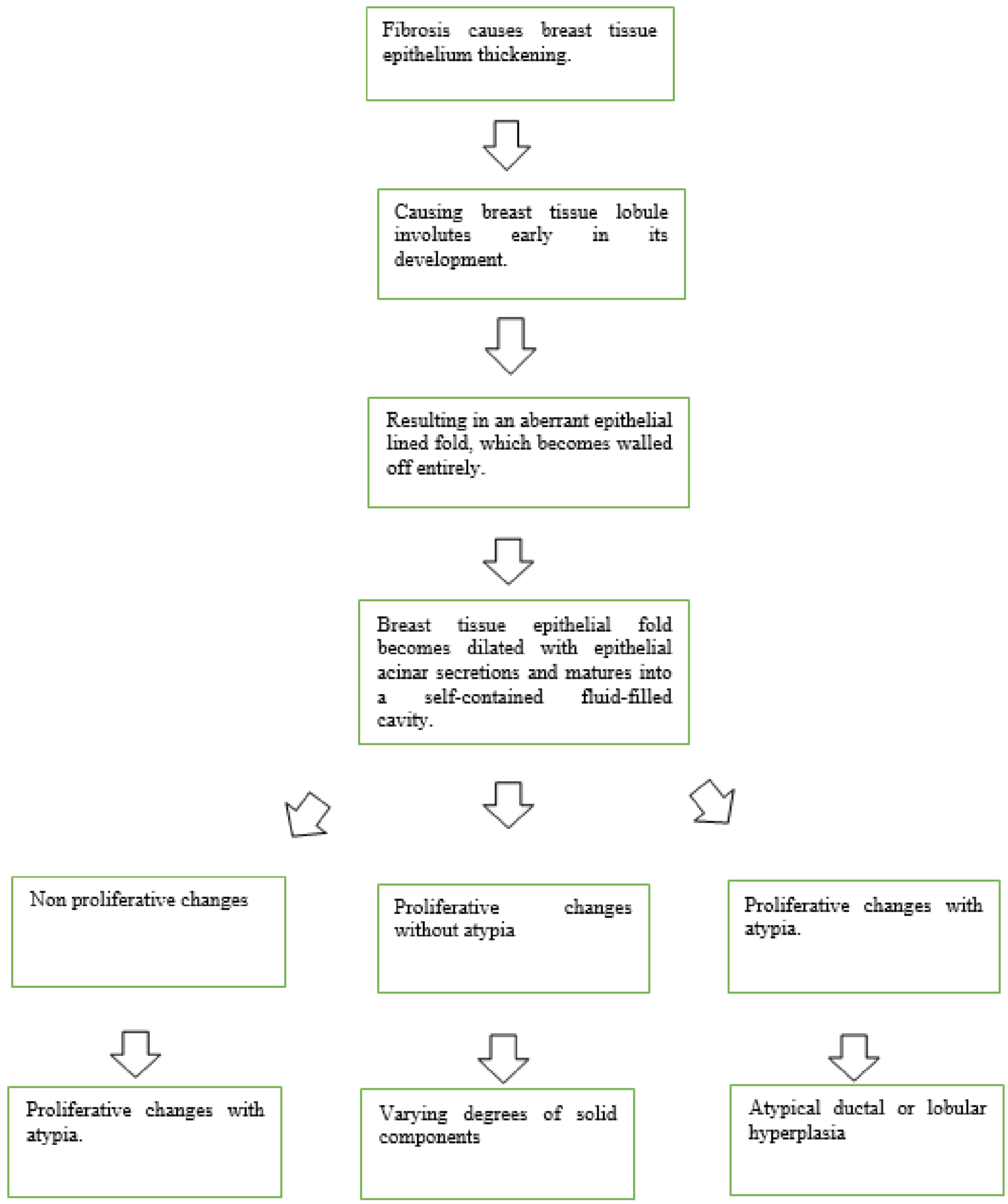

Figure 5: Conceptual framework

2.6 Rational of Study

In view of possibility of malignant transformation of complex breast cysts, it is important to detect specific characteristic of complex breast cyst when performing an ultrasound examination. Hence, the ability of ABVS and HHUS in outlining the characteristic is very crucial, especially in patient with fibrocystic breast disease. Time consuming is one of the limitations in handheld ultrasound, especially when HHUS is performed for patient with multiple breast cysts. Current practice in HUSM is suspicious lesions that detected in ABVS will be assessed again by using HHUS for further characterization. Hence, if we able to detect all the characteristic of complex breast cysts by solely using ABVS without reconfirmation by HHUS, scanning time required for a patient will be drastically reduced. Hence, we can increase the appointment cases either for screening or follow up.

From our literature review, there is no study conducted specifically in comparing characteristics of complex breast cysts in ABVS and HHUS. Thus, the aim of this study is to determine the agreement between ABVS and HHUS in detecting the features of complex breast cysts.

The aim of this study is to determine the agreement between ABVS and HHUS in detecting the features of complex breast cysts which includes thick wall, thick septa and presence of solid component. If the result shows perfect agreement between ABVS and HHUS in detecting features of complex breast cyst, HHUS can be exempted in further characterization of complex breast cysts after performing ABVS. Thus, it will reduce procedure time for each patient and more appointment cases can be added in for one day.

CHAPTER 3: METHODOLOGY

3.1 Study Design

This study will be conducted as a cross sectional study, comparing features of complex breast cysts in HHUS and ABVS.

3.2 Study Population

3.2.1 Reference Population

Patients with complex breast cysts

3.2.2 Target Population

Patients in HUSM who have complex breast cysts.

3.2.3 Source Population

Patients with complex breast cysts who underwent HHUS and ABVS imaging in Radiology Department HUSM.

3.2.4 Sampling Frame

Patients with breast cysts who are under imaging follow up in Radiology Department HUSM and fulfil the inclusion and exclusion criteria.

3.3 Sample Size Calculation

For all objectives, the sample size was calculated using calculation for estimation of agreement by Kappa statistics (Kappa (2 raters) - Estimation using Sample Size

Calculator v2.0, prepared by Dr Wan Nor Ariffin, Unit of Biostatistics and Research Methodology). We expect to obtain a high agreement between ABVS and HHUS in detection of thick septation, thick wall and solid component. Therefore, expected Kappa value of 0.95 were used for all the calculations with 10% margin of error. The prevalence of thick septation, thick wall and solid component were obtained from a previous study (Pongrattanaman and Prueksadee, 2013).

For objective 1 and 2, the prevalence used is 26% and the calculated sample (n) is 49. While for objective 3, the prevalence used is 38% and the calculated sample (n) is 40. The largest sample size was obtained from calculation for objective 1 and 2 (49 lesions). Anticipating 10% dropouts due to technical error, the corrected sample size was 55 lesions.

3.4 Sampling Method

No sampling method applied. All available case which fulfilled inclusion and exclusion criteria will be included.

3.5 Inclusion Criteria

1. Patients with complex breast cysts.

2. Size of cyst which is less than three cm.

3.6 Exclusion Criteria

1. Breast skin disorder that are contraindicated for ABVS such as ulceration on the breast.

2. Inflammatory breast disease

3.7 Research Tools

1. Picture Archieve and Communication System(PACS) version 6.0 SP6 for image acquisition.

2. Acuson S2000 Automated Breast Volume Scanner Ultrasound system (ACUSON S2000 AVBS Product Version 1.0, 2009 – 2013 Siemen Medical Solution USA)

3. Acuson Sequoia Ultrasound System (Software version VA10, 2018 Siemens Medical Solution USA, Inc)

4. Syngo Ultrasound Breast Analysis (sUSBA) (Product version 3.0, software version VA40, 2012-2019 Siemens Medical Solutions USA, Inc)

5. Visual Interaction Assistant for Radiology (Viarads) which is blackboard-based system for diagnostic radiology. Patient data, appointment and radiology reports was stored and displayed in VIARADS.

3.8 Operational Definition

Complex breast cysts are defined as cysts with thick walls, thick septa , intracystic masses, or other discrete solid components (Doshi et al., 2007).

There are four categories of complex cysts depend on morphology (Athanasiou et al., 2014):

I. Cysts with a thick wall (≥ 0.5 mm).

II. Cysts with thick internal septa (≥ 0.5 mm).

III. Predominantly cystic complex masses (more than 50% cystic component).

IV. Predominantly solid complex masses (more than 50% solid components) including peripheral cystic components.

3.9 Data Collection

3.9.1 Patient Recruitment

This is a cross-sectional study that was conducted in HUSM, Kubang Kerian, Kelantan, Malaysia. Data was collected from 3rd October 2021 to 2th October 2023. This study obtained approval from the Human Research Ethics Committee of USM (USM/JEPeM/ 21040346). We included 40 patients with complex breast cyst who had undergone HHUS and ABVS and fulfil the inclusion and exclusion criteria. Data was collected retrospectively and prospectively. Retrospectively, data was collected from pool of patients with complex breast cysts who underwent ABVS and ultrasound breast in Radiology Department HUSM from PACS. Prospectively, consent was taken from the patient that had underwent HHUS breast and noted to have complex breast cyst. Subsequently complementary ABVS was performed in this patient who had complex breast cyst for assessment of the features of the complex breast cyst.

3.9.2 Handheld ultrasound

HHUS breast examination was performed by radiology medial officers with at least two years of experience in radiology service using ultrasound machine with high frequency linear probe. The ultrasound machine that was used in our center was Acuson Sequoia ultrasound. The estimated duration for HHUS is approximately 30 minutes to 1 hour depends on number of lesions. Patient was scanned in supine position with her ipsilateral hand raised above the head. The ultrasound probe was oriented perpendicular to the chest wall. Scanning will be done using radial scanning technique, in a clockwise fashion and using the nipple as a center point. The images of the lesion were taken in two dimensional views (axial and longitudinal) with proper labelling of position of the lesion. Images were saved and sent to PACS. The shape, margin, orientation, echo pattern, posterior features and size were stated in the ultrasound report, according to BI-RADS ultrasound lexicon. There are four categories of complex breast cysts depend on morphology which are cysts with a thick wall (≥ 0.5 mm), cysts with thick internal septa (≥ 0.5 mm), predominantly cystic complex masses (more than 50% cystic component) and predominantly solid complex masses (more than 50% solid components) including peripheral cystic components (Athanasiou et al., 2014). Figure 6 a, b and c show the images for complex breast cyst. The variable taken includes septa, wall and solid component. Thickness of septa which was equal or more than 0.5mm was considered as thick septa, wall thickness than equal or more than 0.5mm was considered thick wall and presence or absence of solid component.

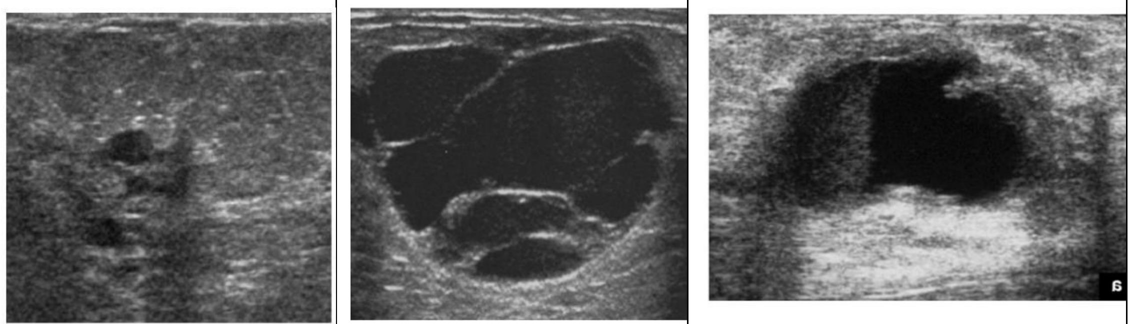

Figure 6a Figure 6b Figure 6c

Figure6: 6a) Type IV complex mass with a solid component of more than 50%, with small peripheral cystic recesses. 6b) Type II complex cystic mass. This is a predominantly cystic mass, with many septa, which are > 0.5 mm thick. 6c) Type III complex mass with predominantly cystic lesion. (Adapted from Athanasiou et al., 2014)

3.9.3 Automated breast volumetric scanner (ABVS)

ABVS the characteristics of complex breast cysts that can be detected in HHUS. The ABVS machine that was used in our center was Acuson S2000 Automated Breast Volume Scanner Ultrasound. The estimated duration for ABVS study / image acquisition is approximately 15 minutes to 30 minutes. Patient will be placed in supine position with supportive cushion at the back. Lotion was applied evenly onto the breast using spatula. Probe was placed over the breast and small pressure was applied to stabilize the breast. Proper cup size preset was selected, and adequate coverage and depth was ensured. Image was acquired and nipple marker was placed over the nipple. The 3D volume data that is recorded was sent from the ABVS to a workstation which is Syngo Ultrasound Breast Analysis (sUSBA). Images was reviewed in multiple orientations using a multiplanar reconstruction (MPR) display. The variable taken includes septa, wall and solid component.

3.9.4 Data Collection:

Age and race of patients as well as size of the lesions were included in the data. The major population in Kelantan is Malay and the majority (90%) of the patients included in this study are Malay. Thus, patients were categorized into Malay and non-Malay group. These data were taken from Viarads and PACS. Images of complex breast cysts in HHUS and ABVS were reviewed. Characteristics of complex breast cysts in each modality were reviewed and compared by principal investigator.

3.9.5 Validation:

Data validation for at least 10% of the total samples was done by the radiologist (research supervisor).

3.10 Satistical Analysis

Data was coded and entered using the statistical package Statistical Package for the Social Sciences (SPSS) version 26. Demographic and clinical characteristics of participants were tabulated in a descriptive table. All numerical variables were presented as mean and standard deviation (SD). For all categorical variables, frequency (n) and percentage (%) were presented. For all objectives, agreement between HHUS and ABVS was estimated using Kappa statistics (unweighted Kappa). The estimated Kappa was presented as the Kappa value, accompanied by its 95% confidence interval. The following classifications had been suggested to interpret the strength of the agreement based on the Cohen's Kappa value (Altman 1999, Landis JR (1977)). Kappa result be interpreted as follows: Kappa value < 0 as indicating poor agreement and 0.01–0.20 as slight, 0.21–0.40

as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement (Assessing agreement using Cohen's kappa,n.d.).

3.11 Confidential and Privacy

All data collection sheet were anonymous and data was entered into SPSS software. The data was presented as grouped data and not identifying the responders individually. Only research team members can access the data. Data was kept in password protected computer to ensure confidentiality.

3.12 Ethical Consideration

The study was approved by Human Research Ethics Committee of Universiti Sains Malaysia (USM/JEPeM/ 21040346).

3.13 Study Flow Chart

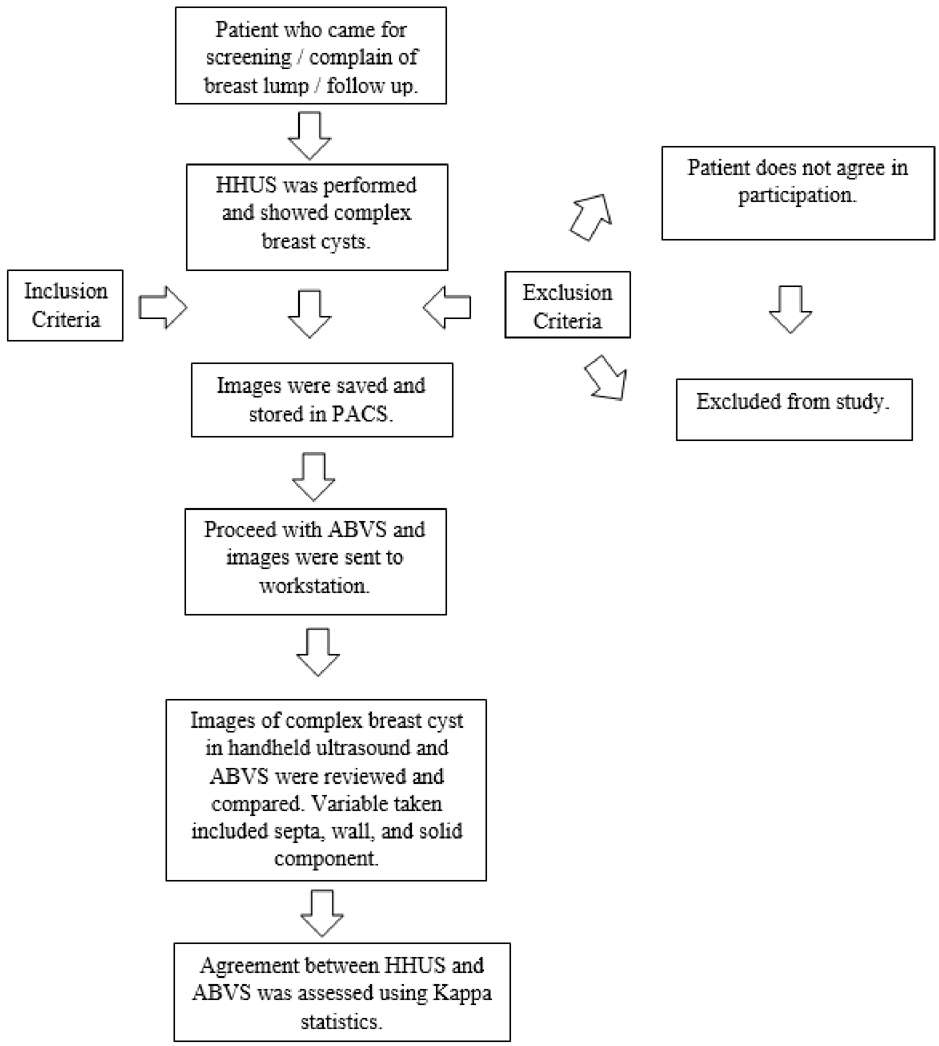

Figure 7: Study flow chart for prospective data collection

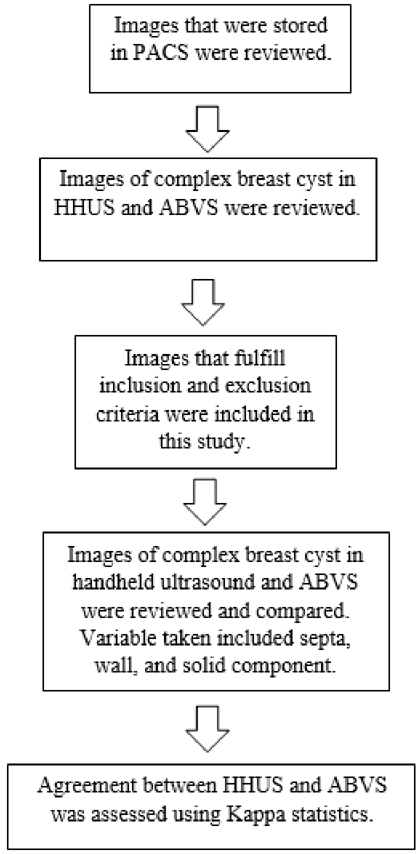

Figure 8: Study flow chart for retrospective data collection