The Breast Ultrasound Elastography And B-Mode Ultrasound for Diagnosing the Breast Lesions in Comparison with Mammography: A Systematic Review

Norliana Mat Rais, Bsc
Department Of Diagnostic Imaging and Radiotherapy, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Jalan Sultan Ahmad Shah Bandar Indera Mahkota 25200 Kuantan, Pahang, Malaysia.
norliana.rais@live.iium.edu.my

***Farah Wahida Ahmad Zaiki, PHD**
Department Of Diagnostic Imaging and Radiotherapy, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Jalan Sultan Ahmad Shah Bandar Indera Mahkota 25200 Kuantan, Pahang, Malaysia.
farahzaiki@iium.edu.my

Corresponding author:
farahzaiki@iium.edu.my

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Abstract:

Background: Breast ultrasound scanning is usually used to complement mammography screening in clinical practice to detect and locate breast lesions. In recent advancements, the breast ultrasound elastography (UE) technique is believed to be able to differentiate the breast lesions between malignant and benign accurately. This paper describes a systematic review of journal articles published from 2010-2020 on the accuracy of breast UE, B-mode ultrasound, and mammography.

Materials and Methods: Four online databases were used to gather published articles and the potential articles were assessed using the Critical Appraisal Skills Programme (CASP) checklists. The final 13 articles identified were cross-checked with the inclusion criteria. These articles were then classified into diagnostic accuracy of mammography, B-mode ultrasound, and breast ultrasound elastography technique.

Result: The results showed that the breast ultrasound elastography technique has high accuracy in differentiating breast lesions. This is mostly acquired when conventional B-mode ultrasound is combined with the shear wave elastography (SWE) technique. Then, the range of area under the receiver operating characteristic curve (AUC) is between 0.903 to 0.972. Likewise, the combination of conventional B-mode ultrasound and mammography screening showed approximately equal diagnostic accuracy. Therefore, this review may serve as a better understanding on the accuracy of the breast elastography technique to distinguish lesions as an alternative to the gold standard; mammography.

Conclusion: This review recommends for further analysis through a meta-analysis to acquire more evidence on figures and statistical analysis. The development of screening protocol studies using UE techniques could also be encouraged in a clinical setting.

Keywords: Breast lesions, diagnostic accuracy, mammography, systematic review, ultrasound elastography, B-mode ultrasound

Introduction:

Two basic concepts currently used in ultrasound elastography (UE) are; the examination of the strain or deformation of tissue due to a force known as static or strain elastography (SE), and the analysis of the propagation speed of shear wave that is the shear wave elastography (SWE). It has been asserted that the breast UE improves the radiologist's interpretation in characterizing the lesions between benign and malignant (Cho et al., 2014 and Song et al., 2018). The quantitative and qualitative measurements used in UE interpretation has demonstrated promising results in accuracy, specificity, and sensitivity.

The common protocol to locate breast lesions is by complementing mammography and breast ultrasound examinations. This combination would put the patient in pain for mammography examination as the breast needs to be compressed for better contrast. For ultrasound examination, it is gentler and safer. In this view, the advancement of ultrasound elastography (UE) may improve the practice of locating and distinguishing breast lesions. Therefore, this systematic review aims to compare the diagnostic performance of breast UE, B-mode ultrasound, and mammography in discriminating the breast lesions between benign and malignant.

Materials and Methods:

The research was approved by the Kulliyyah of Postgraduate and Research Committee (KPGRC) before the review was conducted. Free-text terms combination, controlled vocabulary terms which are Medical Subject Headings (MeSH), and Boolean operators were used during the literature search strategy (Table 1).

These methods were applied in all databases which are PubMed, EBSCOhost, Scopus, and Cochrane Library. MeSH methods were mainly used in the Cochrane Library and the Boolean operator 'OR' was applied to gather broad studies and increase the search results. Then, the operator 'AND' was applied to narrow down the search results. Search results were filtered within a range of 10 years (2010-2020).

Table 1: The literature search strategy

No.	Databases	Search terms used			Number of studies retrieved
1	PubMed	Breast ultrasound elastography			1841
2	EBSCOhost	Shear wave elastography	or		68
3	Scopus	Strain elastography Mammography			172
4	Cochrane Library	Needle biopsy			17
		Breast screening Breast examination	or	and	
		Diagnosing breast lesions Diagnosing breast cancer Diagnosing breast calcifications	or		
Total					2098

The inclusion criteria for the study selection were: (1) prospective cohort and randomized-controlled trial studies; (2) female patients aged 17 years old and above; (3) suspected with breast lesions; (4) index tests were B-mode ultrasound, mammography, and breast ultrasound elastography; (5) histopathological result as a gold standard reference; (6) statistical data with 95% confidence interval; and (7) a full report of the study published in the English language. The critical appraisal and quality assessment to avoid bias was adapted from the Critical Appraisal Skills Programme (CASP) Checklists.

The data extracted from studies selected included, author(s), year of publication, study design and setting, study population, age, number of subjects recruited in study and analysis, and patient selection criteria. Further, the data were index and reference tests characteristics, methods of the test, time interval, cut-off values, statistical data on diagnostic accuracy, and the outcome of the study.

Result:

Literature search

A total of 2,098 reported studies were gathered. At the end, only 13 studies were included for qualitative synthesis as showed in Figure 1. This process involved independent reviewers to avoid bias in the choice of articles.

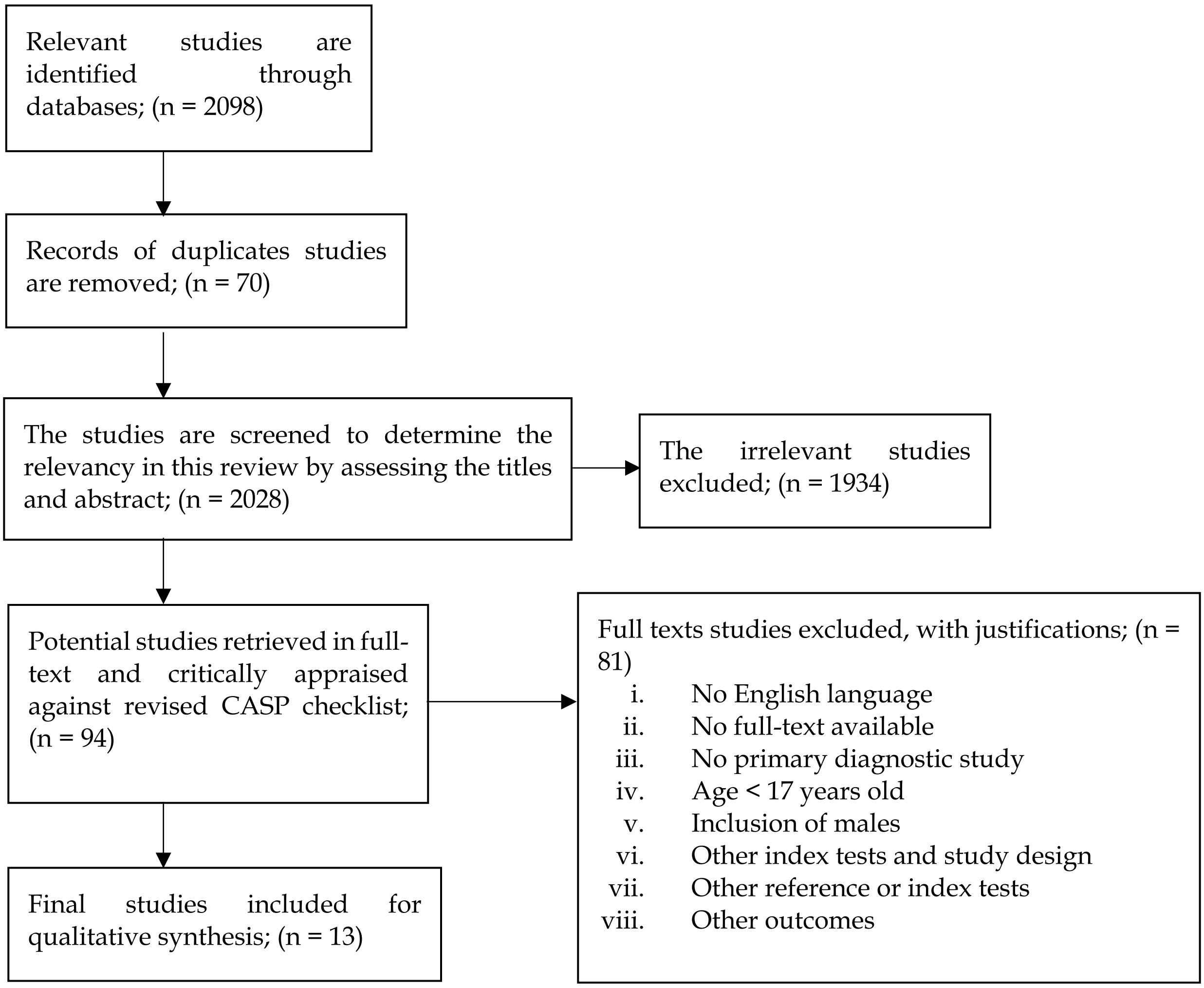

Figure 1: Flowchart for study selection adopted by the Critical Appraisal Skills Programme (CASP) Checklists

Characteristics of included studies

Study and design characteristics

To avoid the occurrence of selection bias in retrospective studies, all studies included in the study were prospective research designs. This review only selected the studies which used conventional B-mode ultrasound, mammography, and UE as the index tests; and confirmation as the reference test.

Based on Table 2, the age of the patients was above 40 years old, and more than 50 female patients were included in the studies. To highlight, Shen et al. (2015) involved 13, 339 female patients in their randomized-controlled trial study.

Among the thirteen studies studies, three studies evaluated the diagnostic performance of ultrasound and mammography to detect breast lesions. The studies were; Berg et al. 2016; Ying et al. 2012; and Shen et al. 2015. Significantly, these studies involved a vast number of patients compared to other studies and the duration of the study ranged from two to eight years. These were due to multiple screenings and follow-up sessions required within the time intervals to detect breast lesions.

The other ten studies investigated the diagnostic performance of UE in discriminating the breast lesions between benign and malignant. A total of 18,369 patients and 1,885 lesions were recorded from the studies by; Ye et al. 2013; Mohamed Hefeda et al. 2019; Au et al. 2014; Lee et al. 2014; Chang et al. 2011; Farooq et al. 2019; Alhabshi et al. 2013; Fausto et al. 2015; Barr et al. 2012; and Gheonea et al. 2011. A total of 1,184 benign and 701 malignant lesions were recorded. Thus, this resulted in 37.2% malignancy rate.

Two methods of UE were included in this review which were SWE and SE. Among the studies, the investigations focused on the optimum quantitative and qualitative values to characterize breast lesions. Namely, the mean elasticity (E_{mean}), maximum elasticity (E_{max}), elasticity ratio (E_{ratio}), the ratio of shear wave velocity between lesions and normal tissue (R-SWV), elasticity score, and width ratio. Along with these, there were two modes of SWE; virtual touch tissue imaging (VTI) and virtual touch tissue quantification (VTQ). This showed that the diagnostic performance of UE was evaluated based on quantitative and qualitative measurements.

Diagnostic accuracy

Some studies investigated the comparison between mammography and ultrasound (Ying et al. 2012; Shen et al. 2015; and Berg et al. 2016). To emphasize, Shen et al. (2015) performed a randomized controlled trial and the other two studies performed a prospective study design. A total of 16,550 patients were recorded in approximately two to eight years of the investigation period. This is important as the longer the period of study, the more reliable the results and observation would be.

In the study by Ying et al. (2012), 246 malignant and 419 benign lesions were recorded. Respectively, the sensitivity recorded for mammography and ultrasound was 81.71% and 95.53%. The specificity values for mammography and ultrasound were 85.44% and 80.43% respectively. In the assessment for accuracy of mammography and ultrasound, diagnostic accuracy assessment (AUC) reported were 0.886 ± 0.016 and 0.948 ± 0.010 respectively.

Based on the randomized-controlled trial by Shen et al. (2015), 4,447 women were randomized into a group that used the combination of mammography and ultrasound screenings which consisted of 6,916 benign and 14 malignant lesions. AUC for this combination screenings were 0.7666 and 0.999 respectively. To be specific, mammography reported having 57.1% sensitivity and 100.0% specificity. By contrast, the ultrasound had 100.0% sensitivity and 99.9% specificity. Meanwhile, a study by Berg et al. (2016) evaluated the performance of mammography and ultrasound with patients having a range of 26% to 40% breast density. Consequently, the sensitivity recorded for mammography and ultrasound were 64.7% and 52.9% respectively. On the other hand, both imaging modalities recorded 56.3% sensitivity for breast density higher than 80%.

Table 2: Characteristics of included studies

Author(s)	Setting	Study design	No. of patient	Mean age	Diagnostic imaging	No. of lesions analyzed
Berg, W. A., et al. (2016)	Chicago	Prospective	2662	NA	US and mammography	NA
Ying, X., et al. (2012)	China	Prospective	549	46	US and mammography	665
Shen, S., et al. (2015)	China	Randomized-controlled trial	13, 339	46.4	US and mammography	NA
Ye, L., et al. (2013)	China	Prospective	75	42	Ultrasound elastography	186
Mohamed Hefeda, M., et al. (2019)	Egypt	Prospective	142	49	Ultrasound elastography	142
Au, F. W. F., et al. (2014)	Canada	Prospective	112	49.2	Ultrasound elastography	123
Lee, S. H., et al. (2014)	Korea	Prospective	207	45.5	Ultrasound elastography	207
Chang, J. M., et al. (2011)	Korea	Prospective	158	48.1	Ultrasound elastography	182
Farooq, F., et al. (2019)	Pakistan	Prospective	155	45.41	Ultrasound elastography	155
Alhabshi, S. M. I., et al. (2013)	Malaysia	Prospective	186	48	Ultrasound elastography	168
Fausto, A., et al. (2015)	Italy	Prospective	147	52	Ultrasound elastography	129
Barr, R. G., et al. (2012)	USA	Prospective	578	56	Ultrasound elastography	635
Gheonea, L., et al. (2011)	Romania	Prospective	58	45.3	Ultrasound elastography	58

Referring to Table 3, SWE and SE techniques showed higher diagnostic accuracy performance. The studies by Ye et al. 2013; Au et al. 2014; Farooq et al. 2019; Fausto et al. 2015 and Gheonea et al. 2011 reported nearly 100% of AUC. Among these studies, Farooq et al (2019) reported the highest AUC which was 0.972 with $E_{mean} \leq 72$ kPa cut-off value using the shear wave elastography method. The second highest AUC was by Au et al (2014) which reported an AUC of 0.932 with 42.5 kPa E_{mean} cut-off value. The same study presented 0.931 and 0.943 of AUC value with E_{max} and E_{ratio} respectively. Here, the cut-off values involved were 46.7 kPa and 3.56 respectively.

A study by Gheonea et al. (2011) used strain elastography and acquired 0.965 AUC value with E_{ratio} cut-off value of 3.67. This was followed by Fausto et al (2015) with AUC 0.94 resulting from E_{ratio} cut-off value of 3.3. Next, a study by Ye et al. (2013) reported an AUC value of 0.903 using virtual touch tissue quantification (VTQ) cut-off value of 4.65 m/s, and the value of AUC for R-SWV with cut-off 5.18 was 0.918. The qualitative AUC value also reported higher than quantitative measurements. Particularly, the value was 0.939 with 1.1 cut-off value.

However, a study by Mohamed Hefeda et al. (2019) had not presented the qualitative AUC measurement for SWE acoustic radiation force impulse (ARFI) and SE elasticity scores. Though these were not presented in the study, respective sensitivity and specificity were 92.42% and 92.11% for the ARFI elasticity score. Meanwhile, sensitivity and specificity for SE elasticity score were 83.1% and 88.73% respectively. The remaining studies also reported sensitivity and specificity percentages above 80%. In short, the above details showed that the UE parameters are reliable alternative methods to differentiate the types of breast lesions.

Table 3: Diagnostic performance of included studies

B-mode/UE technique	Diagnostic measurement	Cut-off value	Sensitivity (%)	Specificity (%)	AUC
B-mode	NA	NA	80.82	88.41	NA
B-mode	NA	NA	97.73	35.44	NA
B-mode	NA	NA	97	61.4	0.792
SWE	VTI	1.1	93	89	0.939
SWE	VTQ	4.65 m/s	81	97	0.903
SWE	VTQ (SWV)	NA	94.03	95.95	NA
SWE	R-SWV	5.18	82	96	0.918
SWE	E_{mean}	42.5 kPa	88.64	89.87	0.932
SWE	E_{mean}	50	98.9	66.7	NA
SWE	E_{mean}	80.17	88.8	84.9	NA
SWE	E_{mean}	100	80.9	88.3	NA
SWE	E_{mean}	≤ 72	92.17	90.4	0.972
SWE	E_{max}	46.7 kPa	90.91	88.61	0.931
SWE	E_{ratio}	3.56	86.36	93.67	0.943
SWE	ARFI Elasticity score	NA	92.42	92.11	NA
SE	E_{ratio}	NA	94	72	NA
SE	E_{ratio}	3.3 au	88	87	0.94
SE	E_{ratio}	< 1.0 ≥ 1.0	98.6	NA	NA
SE	E_{ratio}	3.67	93.3	92.9	0.965
SE	Width ratio	NA	91	88.1	NA
SE	Width ratio	1.1	97	84	NA
SE	Elasticity score	NA	83.1	88.73	NA

In ten included studies, three studies compared the diagnostic performance of the combination of ultrasound and elastography (Alhabshi et al. 2013; Chang et al. 2013; and Au et al. 2014). The percentage of sensitivity and specificity recorded was high when the quantitative measurements were applied as clearly demonstrated in Table 4. The study by Au et al. (2014), combined the B-mode conventional ultrasound with SWE cut-off parameters. The sensitivity and specificity from this study were, 95.45% and 84.81% respectively with 42.5 kPa cut-off value of E_{mean}. Furthermore, the ultrasound also combined with 46.7 E_{max} cut off value. This produced 95% and 83.54% of sensitivity and specificity, respectively. The last combination in this study was with the E_{ratio} of 3.56. The sensitivity and specificity were 95.45% and 87.34%, respectively. The significance for these combinations was accordingly 0.901, 0.895, and 0.914.

In the study by Chang et al. (2013), it was reported that the combination of B-mode ultrasound with 80.17 kPa SWE E_{mean} cut otff value produced 0.946 of AUC. Meanwhile, the study by Alhabshi et al. (2013) used the combination of B-mode ultrasound and SE. The sensitivity and specificity reported were 100% and 90% when the width ratio of 1.1 is used.

Table 4: Combination of conventional ultrasound with elastography parameter diagnostic performance

Scanning	Cut off value	Sensitivity (%)	Specificity (%)	AUC
US alone	NA	97.73	35.44	0.666
US + E_{mean}	E_{mean}, 42.5 kPa	95.45	84.81	0.901
US + E_{max}	E_{max}, 46.7	95.45	83.54	0.895
US + E_{ratio}	E_{ratio}, 3.56	95.45	87.34	0.914
US + E_{mean}	E_{mean}, 80.17	NA	NA	0.982
US + UE	NA	100	90	0.946

Discussion:

Prominently, it was found that the UE produced high diagnostic accuracy in differentiating breast lesions. This is supported by studies that investigated elastography accuracy using various cut-off parameters quantitatively and qualitatively. Moreover, the combination of conventional B-mode ultrasound and parameters of elastography increased the significance of the diagnostic performance. Especially when applied with the SWE quantitative parameter which is E_{mean}.

Across all included studies, there was less quantitative diagnostic measurement applied in the SE studies. By this, it demonstrated that the SWE method was more preferred than SE. This may be because the SE is highly dependent on the compression applied by the operator to the tissue (Yu et al., 2018). As a result, it is difficult to reproduce scanning for the same patient at different serial monitoring or between different patients. Unlike this, the SWE method depends less on the individual operator and is highly reproducible for every scanning (Kim et al., 2015).

Fewer studies were performed to classify breast lesions using qualitative elastography. The reason is, the qualitative measurement is subjective to the operator's observation and interpretation of the elastography score and color pattern of the lesions. Consequently, this may lead to inconsistency of diagnosis and later affect the patient's health condition. Among the thirteen studies, only two studies evaluated the performance of qualitative diagnostic measurement in differentiating malignant and benign lesions (Ye et al., 2013; and Mohamed Hefeda et al., 2019).

In another view, the combination of conventional B-mode ultrasound and mammography was found to produce the same high diagnostic accuracy as the combination of B-mode and elastography technique based on studies performed by Alhabshi et al. (2013); Au et al. (2014) and Shen et al. (2015). The study by Shen et al. (2015) was the most reliable as they performed a randomized controlled trial which is the second-highest level of evidence with a large number of participants. Also, this strengthens the reason why ultrasound examination should complement mammography examination. As well, this demonstrated that breast UE can potentially be performed independently and is also safer and can reduce anxiety compared to a mammography examination.

Furthermore, this review is complimented by other systematic reviews. According to Liu et al. (2016), "the SWE is a reliable and non-invasive procedure that can be easily integrated into the current imaging protocols." Here, their meta-analysis assessed quantitative diagnosis using ultrasound shear wave elastography. More recently, a diagnostic meta-analysis performed by Luo et al. (2018) significantly asserted that SWE truly improved the diagnosis of breast lesions between benign and malignant. Nevertheless, considering evolving technologies in imaging modalities as part of our limitation, latest technologies are suggested to have higher diagnostic accuracy.

Conclusion:

The elastography technique is an outstanding method to detect and characterize breast lesions without being highly dependent on using ionization radiation and invasive biopsy methods. This technique has shown to have higher diagnostic accuracy over conventional ultrasound alone. The comparison of combination methods between conventional ultrasound with mammography and conventional ultrasound with elastography also showed a significant result. Accordingly, it denotes less difference between the two combinations. Therefore, we deem that breast UE is a promising alternative method to detect and characterize the types of breast lesions. It also reveals the potential for breast UE to be used independently without supplementing with mammography screening. Given this, we observed that this review can be elaborated further through the conduct of a meta-analysis to acquire more statistical evidence. This would provide more significant results on the ability of ultrasound, mammography, and UE techniques to discern between benign and malignant breast lesions. Finally, we recommended that more studies on developing the screening protocol using UE techniques be considered.

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