Diagnostic Performance of Solid Breast Lesions Shearwave Elastography with Histopathological Correlation

By:

Dr Siti Hajar binti Omar

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TABLE OF CONTENT

Content **Page**

LIST OF FIGURES

LIST OF TABLES

ABBREVIATION

ACR	American College of Radiology
BI-RADS	Breast Imaging Reporting and Data System
COV	Cut-off value
Emax	Maximum stiffness
Emean	Mean stiffness
FNAC	Fine Needle Aspiration and Cytology
HPE	Histopathological examination
kPa	kilopascal
NCR	National cancer registry
NPV	Negative predictive value
PACS	Picture Archiving Computer System
PPV	Positive predictie value
ROC	Receiver operating characteristic
ROI	Region of interest
SD	Standard deviation
SWE	Shearwave elastography
WHO	World Heath Organization
WISH	Women’s Imaging Suite

ABSTRACT

Introduction: Shearwave elastography (SWE) is an emerging technique of obtaining quantitative tissue elasticity data during breast ultrasound examinations.

Objectives: The aim of this study were (1) to determine the mean of maximum SWE value of malignant and benign breast lesions (2) to determine the sensitivity and specificity of SWE correlating with histopathology (3) to determine the agreement between SWE and greyscale ultrasound in differentiating malignant and benign breast lesions.

Methodology: Using the Aixplorer® ultrasound system 174 solid breast lesions were identified using us. For each lesion, quantitative elasticity was measured and BI-RADS categories assessed with greyscale. SWE maximum value was calculated and compared with the previously published cut-off value (COV). SWE measurements were correlated with histology results. Greyscale images according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) categories 1-3 were taken as benign while categories 4-6 were classified as malignant.

Results: Of the 174 breast lesions, 149 (85.6 %) were benign and 25 (14.4%) were malignant revealed by histology. The mean of maximum elasticity values were significantly higher in malignant lesions (98.00 kPa ± 50.39) than benign lesions (28.16 kPa ± 17.22), (P < 0 .001).

The optimal SWE cut-off value was 42.58 kPa with sensitivity and specificity of SWE were 84.0% and 81.0%, positive predictive value (PPV) and negative predictive value (NPV) were 42.0% and 97.0% respectively. The AUC of ROC curve was 0.864 for greyscale ultrasound, 0.824 for SWE, and 0.773 for combined greyscale and SWE.

There was moderate agreement between results from BI-RADS with COV of 3.5 and SWE of the three COVs. The Kappa agreement between BI-RADS and SWE was increased from

0.458 to 0.550, as the SWE COV increased from 42.58 kPa to 50.0 kPa and 80.0 kPa. Overall, the highest agreement was obtained between BIRADS (COV=3.5) and SWE (COV=80 kPa).

Conclusions: Malignant breast lesions have higher maximum SWE value compared to benign lesions . The overall diagnostic performance of combination grey scale ultrasound and SWE was not significantly better than that of ultrasound alone. The optimum COV of SWE obtained from this study was lower than the previous studies, however one might choose higher COV in order to increase the specificity of this potential adjunct screening and diagnostic tool particularly in BI-RADS III or IV breast lesion.

ABSTRAK

Pengenalan: Shear wave elastography (SWE) merupakan teknik pemeriksaan sonografi yang terkini, dimana ia dapat memberi nilai pemeriksaan ultrasound payudara secara kuantitatif.

Objective: Tujuan kajian ini adalah (1) untuk menentukan nilai purata SWE bagi ketumbuhan kanser dan bukan kanser payudara (2) untuk menentukan sensitiviti dan ketepatan teknik SWE dalam menentukan ketumbuhan kanser dan bukan kanser payudara dimana keputusan akan dibandingkan dengan histologi (3) untuk menentukan persetujuan antara pemeriksaan SWE dan sonografi konvensional dalam membezakan bagi ketumbuhan kanser dan bukan kanser payudara

Kaedah: Seramai 174 orang wanita yang mempunyai ketumbuhan payudara telah menjalani pemeriksaan ultrasound dan SWE dengan menggunakan mesin Aixplorer® ultrasound system (SuperSonic Imagine, Aix en Provence, France). Bagi setiap ketumbuhan payudara, nilai SWE dan ciri-ciri morfologi yang telah dikategorikan menggunakan BI-RADS telah dianalisa.

Prestasi diagnostik bagi parameter SWE telah dianalisa dan dibandingkan dengan had nilai SWE yang diperoleh daripada kajian yang terdahulu. Analisa sonografi konvensional bagi ketumbuhan payudara telah dikategori menggunakan BI-RADS. Kategori 1-3 untuk ketumbuhan bukan kanser payudara, mankala kategori 4-6 untuk ketumbuhan kanser payudara.

Keputusan: Daripada 174 ketumbuhan payudara yang telah diperiksa, sebanyak 149 (85.6 %) adalah ketumbuhan bukan kanser dan sebanyak 25 (14.4%) merupakan kanser yang telah dipastikan melalui keputusan histologi. Nilai had SWE yang paling optimum untuk membezakan ketumbuhan kanser dan bukan kanser ialah 42.58 kPa dimana ia memberi tahap sensitiviti dan ketepatan sebanyak 84% dan 81.0%, manakala nilai prediksi positif dan nilai prediksi negative ialah 42% dan 97% masing-masing. Kawasan dibawah lengkungan ROC yang tertinggi ialah 0.864 untuk ultrasonografi konvensional. Terdapat persetujuan yang sederhana di antara kedua-dua pemeriksaan ultrasonografi konvensional dan SWE bagi nilai-nilai had yang ditetapkan. Persetujuan yang tertinggi ialah di antara BI-RADS (COV=3.5) dan SWE (COV=80 kPa).

Konklusi: Nilai maximum SWE bagi ketumbuhan kanser payudara adalah lebih tinggi berbanding ketumbuhan bukan kanser. Secara keseluruhannya, pemeriksaan SWE berpotensi sebagai pemeriksaan sampingan bagi membezakan ketumbuhan kanser payudara dan bukan kanser, namun demikian, kajian ini gagal membuktikan prestasi diagnostik pemeriksaan SWE ini dapat mengatasi prestasi diagnostik ultrasound konvensional. Nilai had optimum SWE yang diperolehi daripada kajian ini adalah lebih rendah berbanding dengan kajian-kajian terdahulu. Walaubagaimanapun, nilai had SWE yang lebih tinggi boleh ditetapkan untuk meningkatkan nilai ketepatan pemeriksaan SWE untuk membezakan ketumbuhan payudara kanser dan bukan kanser terutamanya bagi kes BI-RADS III dan IV.

Introduction

Breast cancer is a widespread problem and remains the most common malignancy in females worldwide. It is also the first most common cancer among population regardless of sex in Malaysia. There were 3,242 female breast cancer cases diagnosed in 2007 and reported to NCR (National cancer registry) of Malaysia, accounted for 32.1% of all female cases (Zainal Ariffin and Nor Saleha, 2011). Therefore, screening for early detection of breast cancer is crucial and has become a big challenge in medical field.

Greyscale ultrasound has a long-established role in the assessment of symptomatic breast masses. A sonographic BI-RADS lexicon was used to provide standardized terminology to facilitate accurate and consistent breast sonography and mammography reporting as well as a widely accepted risk assessment. The sonographic BI-RADS descriptors of malignancy include spiculated margin, irregular shape, and nonparallel orientation whereas circumscribed margin, oval shape, and parallel orientation were descriptors for benign lesion. The sonographic BI-RADS lexicon showed 71.3% accuracy, 98.1% sensitivity, 32.9% specificity, 67.8% PPV, and 92.3% NPV. The NPV for class 3 was 92.3%. The PPVs for classes 4 and 5 were 46.6% and 87.3% (Costantini et al., 2006). It is a valuable adjunct to mammography as it is non-invasive and non-radiation tools examination. However, it is known to suffer from unavoidable limitation of low specificity (Corsetti et al., 2006).

In the last 10 years, different sonographic methods have been developed to determine the sonographic features of benign and malignant breast lesion in order to increase the sensitivity in detecting malignant breast lesion. This includes the most recent advancement in assessment of tissue elasticity.

Generally, breast cancer tissue is harder than the adjacent normal breast tissue. This property was the basis for some examinations that are being used in the clinical assessment of breast abnormalities, such as palpation as well as for ultrasound elastography assessment. A study by Itoh et al. (2006) shown that ultrasound elastography has nearly the same diagnostic performance as greyscale ultrasound, with 86.5% sensitivity, 89.8% specificity, and 88.3% accuracy in the differentiation of benign from malignant solid breast lesions. However, ultrasound elastography with freehand compression has several disadvantages as it is highly dependent on the surrounding mechanical properties resulting in a substantial amount of interobserver variability during data acquisition and interpretation (Regner et al., 2006). In addition, it only provides qualitative measurement of the tissue elasticity rather than quantitative value.

To overcome this problem, the quantitative elastography technique of shearwave elastography (SWE) has been developed for the past couple of years. SWE allows qualitative as well as quantitative assessment of breast lesions. Unlike conventional or strain elastography methods, which rely on manual compression and measure tissue displacement, SWE does not require manual compression and computes true tissue elasticity by measuring the velocity of shear waves as they propagate in tissue. The system itself induces mechanical vibrations by using an acoustic radiation force created by a focused ultrasound beam. A very fast (5000 frames/s) ultrasound acquisition sequence is used to capture the propagation of the shearwaves. The displacement induced in a breast lesion creates a shearwave that provides information about the local elasticity properties of the tissue and enabling the production of a two-dimensional map of shear elasticity which can be quantify in kilopascal (kPa) (Bercoff et al., 2004; Fink and Tanter, 2010).

The technique was highly reproducible; the intraclass correlation coefficient was 0.8, indicating moderated agreement (Evans et al., 2010). Therefore, SWE could be a valuable adjunct tool in differentiating benign and malignant breast lesions. Within a given region-of-interest (ROI), a variety of stiffness parameters can be measured, including the mean stiffness

(Emean), maximum stiffness (Emax), and standard deviation (SD). There were few earlier studies that used different cut-off value (COV) to determine benign and malignant breast lesion. A study by Evans et al. (2010) used the COV which was taken from the mean elasticity value of 50kPa. Whereas Chang et al. (2011b) used the COV of maximum elasticity of as 80kPa. At this COV, the SWE has sensitivity and specificity of 88.8% and 84.9% respectively.

Since stiffness is a continuous variable, different COV could be chosen. For example, if improved specificity was desired, a higher COV could be used but the cost would be a reduction in sensitivity. Therefore we hope to determine the optimum COV of maximum elasticity for breast cancer in our local population as well as the sensitivity and specificity of SWE for solid breast lesion. This study would have a great impact and benefit to the society as the addition of SWE in ultrasound breast examination might help to differentiate between benign and malignant masses. This may in turn allow a larger proportion of women with benign masses to be reassured and to reduce the number of women subjected to biopsy or short-term follow-up for benign-appearing solid breast lesions.

The general objective of this study was to determine the correlation of SWE solid breast lesions with histopathological findings. The specific objective of this study were (1) to determine the mean of maximum elasticity value of malignant and benign breast lesions (2) to determine the sensitivity and specificity of shear wave elastography correlating with histopathological findings (3) to determine the agreement between SWE and BI-RADS scoring differentiating malignant and benign breast lesions.

Rationale of the study

It is very crucial for early detection of malignant case of breast disease at it is currently the most common cancer in among the population in our country. With new advancement, a new technique of shear wave study was developed but still under limited study especially in Asian population. Therefore, the purpose of this study is to determine the sensitivity and specificity of shearwave elastography for solid breast lesion and the cut off value of maximum elasticity for breast cancer in local population. In a previous preliminary study, a 50-kPa cut-off was derived from the initial 10 patients and then was prospectively applied to 53 further patients (Evans *et al.*, 2010). Use of this cut-off for mean elasticity resulted in a sensitivity of 97% and a specificity of 83%. However, since stiffness is a continuous variable, different cut-off values could be chosen. For example, if improved specificity was desired, a higher cut-off could be used but the cost would be a reduction in sensitivity. Therefore, this study is to determine the optimum cut off value for local population with different demographic background and different prevalence of breast cancer in our country. In addition, there are limited studies being performed in Asia and specifically in our country regarding the diagnostic performance of shearwave elastography on breast lesion which the results may be influenced by the difference in the genetic background.

This study would have a great impact and benefit to the society as the addition of shear wave elastography in ultrasound breast examination to differentiate between benign and malignant masses. This may in turn allow a larger proportion of women with benign masses to be reassured and to reduce the number of women subjected to biopsy or short-term follow-up for benign-appearing solid breast masses.

STUDY PROTOCOL

PROPOSAL FOR DISSERTATION PROTOCOL

In Partial fulfilment of Master of Medicine (Radiology)

TITLE:

Diagnostic Performance of Solid Breast Shearwave Elastography with Histopathological Correlation

By:

Dr Siti Hajar binti Omar

Supervisor: Dr Nik Munirah Binti Nik Mahdi

INTRODUCTION & LITERATURE REVIEW

Breast cancer was the commonest cancer among Malaysian women. In a 3 year period from 2003-2005, 11952 new cases were reported to the National Cancer Registry. Breast cancer accounted for 31.3% of the total number of the new cases in women, with a similar percentage in each of the major ethnic group; Malay (33.6%), Chinise (30.6%) and Indian (31.2%). The age-standardized rate for female was 47.4 per 100,000 women (Hisham and Yip, 2004). Therefore, early detection of breast cancer is crucial. The evaluation of a patient with breast lesion should begin with symptoms and a general clinical history followed by triple assessment, which includes the following components, clinical evaluation, imaging and biopsy. This approach is in order to obtain the diagnosis with the minimum degree of invasiveness and to minimize discomfort to the patient. The aim of evaluation of a breast lesion is to judge whether surgery is required and, if so, to plan the most appropriate surgery.

The most non-invasive and non-radiation tools of examination is breast ultrasound. It can be a valuable adjunct to mammography however, it is known to suffer from the as yet unavoidable limitation of low specificity (Berg, 2004) and (Corsetti et al., 2006) . In the last 10 years, different sonographic methods have been developed to determine the relationship between different structures and their tissue elasticity as well as the potential use of this relationship for diagnosing malignant tumors.

Elastography has been shown to improve the specificity for solid masses in the breast as tissue stiffness or elasticity of breast cancers is known to be harder than that of benign masses (Gweon et al., 2013) and (Evans et al., 2010). Therefore, the breast elastography as a method of imaging tissue stiffness has been used to improve diagnostic confidence and increase the specificity of ultrasound interpretation.

Shear-wave elastography (SWE; SuperSonic Imagine, Aix-en-Provence, France) is a more recent method uses the radiation force induced by the ultrasound push pulse generated by the ultrasound transducer (Athanasiou et al., 2010). This force induces mechanical waves, including shear waves, which propagate transversely in the tissue. The production of the radiation force by the probe rather than the operator means that the SWE is more operator-independent, reproducible, and quantitative (Athanasiou et al., 2010) and (Cosgrove et al., 2012). The SWE allows measurement of the propagation speed of shear waves within the tissue to locally quantify its stiffness in kilopascals (kPa) or meters per second (m/sec). Within a given region-of-interest (ROI), a variety of stiffness parameters can be measured, including the mean stiffness (Emean), maximum stiffness (Emax), and standard deviation (SD).

Shearwave elastography allow qualitative and quantitative assessment on breast lesion according to the elasticity measurement. In previous study done by (Chang et al., 2011) note that the cut-off point of maximum elasticity is taken as 80kPa. At this cut off point, shearwave elasticity has sensitivity and specificity of 88.8% and 84.9% respectively. However, there are limited studies being performed in Asia and specifically in our country regarding the diagnostic performance of shearwave elastography on breast lesion which the results may be influenced by the difference in the genetic background.

RESEARCH QUESTIONS

1. What is the mean elasticity value of benign and malignant breast lesions?
2. What is the sensitivity and specificity of shearwave elastography for malignant and benign breast lesions?
3. What is the correlation of SWE and grey scale USG method in differentiating malignant and benign breast lesion?

RESEARCH HYPOTHESIS

Shear wave elastography is sensitive and specific for malignant breast lesions.

GENERAL OBJECTIVE

To determine the correlation of shear wave elastography solid breast lesions with histopathological findings.

SPECIFIC OBJECTIVES

1. To determine the mean elasticity value of malignant and benign breast lesions.
2. To determine the sensitivity and specificity of shear wave elastography correlating with histopathological findings.
3. To determine the agrement between SWE and grey scale ultrasound in differentiating malignant and benign breast lesions.

METHODOLOGY

Study design: Cross sectional study
Source population: Hospital USM, Kubang Kerian, Kelantan.
Referral Population: Woman with solid breast lesion
Subject/Sampling method: All patients who come for ultrasound examination for solid breast lesion, therefore no sampling method applied
Frame: 2014-2015

Study population

Inclusion criteria

1. Age more than 18years old
2. Female with solid breast lesion

Exclusion criteria

1. Patient who recently had operation on the ipsilateral breast.
2. No histopathology examination result available.

Sample size calculation

Objective 1

Calculate 2 means formula using Power and Sample Size Calculation software version 3.0.10.

- Malignant breast lesion
- Benign breast lesion
  - α: 0.05 Δ:100
  - σ: 58 m:90:10

The highest calculated sample size was 35. However after considering a 10% drop-out, the final sample size for each group is 42.

Objective 2

Using the sensitivity and specificity software

- Expected sensitivity : 88%
- Expected specificity: 84%
- Expected prevalence: 20%
- Desired precision: 0.1
- Confidence level: 95%

- **Samples for sensitivity and specificity**
  - **206** and 47

The sample size calculation was discussed with Dr Wan Ariffin 21.10.2014

Research tools

Aixplorer ultrasound system (SuperSonic Imagine. Aix en Provence, France)

Data Collection:

All patients who come for ultrasound examination for solid breast lesion, fulfilled the inclusion criteria and volunteered for the study will be recruited in this study.

Both conventional grey scale ultrasound and shearwave elastography will be performed in the same setting. Images and data will be saved into Picture and Archiving Computer System (PACs). Data will be retrieved from the PACs and correlation with the histopathological findings is made.

Methodology for Shearwave elastography examination

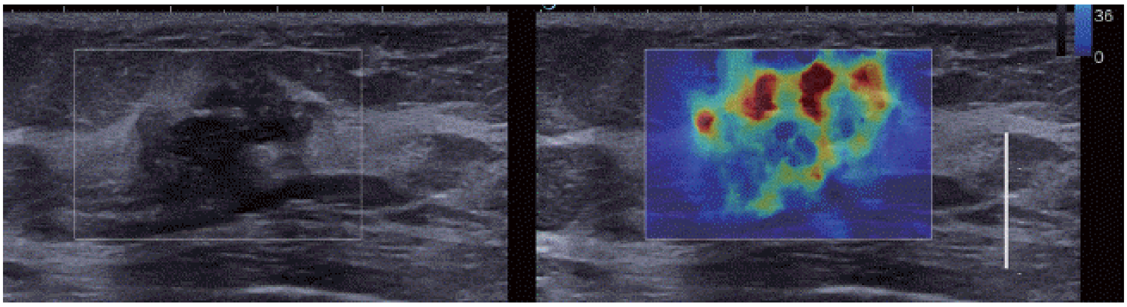
1. Patient needs to be positioned in semirecumbent position with a firm pillow under the back of the examination side.
2. Each patient will undergo a conventional grey scale ultrasonography of both breasts using the Aixplorer ultrasound system (SuperSonic Imagine) with 18MHz linear transducer. Assessment of the breast lesion according to WHO protocol will be performed ie; two orthogonal image for each lesion, assess for the size, margin, echogenicity, presence of calcification.
3. Subsequently, shear wave elastography performed. Elastography application selected. The transducer is held still over the lesion for about 5s to allow the image to build up and patient is asked to breathe slowly. No pressure is applied.

4. The Q box is placed over the stiffest area and the quantitative elasticity values will be obtained automatically by moving the delineated Q box over the colour map.
5. Images will be recorded in Picture Archiving Computer System (PACS) for retrieval and the breast lesion is classified using BIRADS classification.
6. All patients who were referred for ultrasound for solid breast lesions (except for those who has undergone earlier FNAC/trucut biopsy either by pathologist or surgeon) will be subjected for ultrasound guided percutaneous biopsy in the radiology department which will be performed by MMED radiology under radiologist supervision.

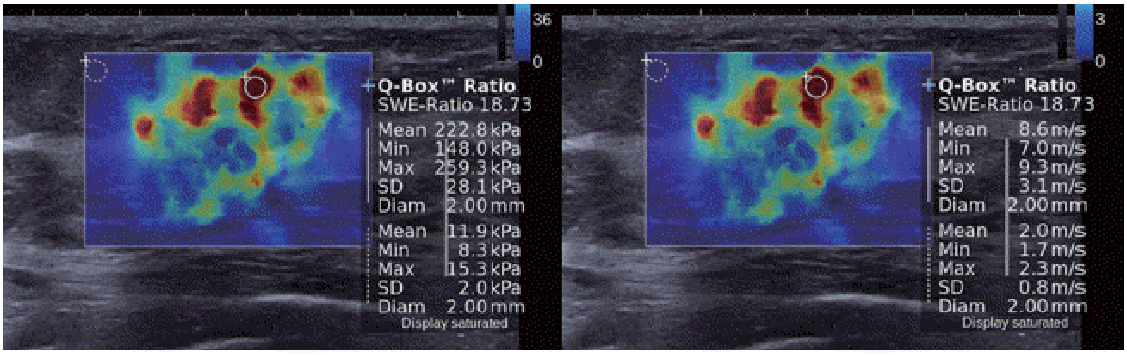
   Generally, either pathologist/surgeon can perform FNAC/biopsy of the palpable breast lesions. However, patients with non-palpable or inadequate sample will be referred to radiologist for biopsy under ultrasound guidance. In addition, the biopsy is also performed by radiology team if the patient came for ultrasound in the initial work up.

7. Sample sent for histopathological assessment.
8. All the procedure will be done in one visit.

Shearwave elastography of breast lesion.



A



B

Validation test

It will be performed at the initial of the study to validate the technique of the researcher in performing conventional ultrasound and shearwave elastrography study. Observers that involved in the validation test are the researcher and validated by a senior consultant radiologist with 11 years of working experience and subspecialty in breast imaging. The researcher will perform conventional ultrasound and shearwave elastrography study on a patient and the examination is repeated in the same setting by the radiologist. Images will be stored in PACS system. Data will be entered in SPSS system and analysed.

Image Analysis

Images obtained on conventional ultrasound will be scored according to the Breast Imaging Recording and Data System (BI-RADS) criteria for ultrasound.

- Grade I – normal;
- Grade II – benign;
- Grade III – probably benign;
- Grade IV – probably malignancy;
- Grade V – highly suggestive of malignancy
- Grade VI – histopathologically proven malignancy

- The characteristics considered were size, shape, margin, orientation, internal echogenicity, presence/absence of calcification, posterior acoustic shadowing, and presence/absence of lymph node enlargement, presence/absence of intra-tumoral blood flow

For shearwave elastrography, the maximum and mean elasticity value of the solid breast lesion will be taken in two readings and mean value will be calculated.

Statistical analysis

1. Descriptive analysis is used to calculate the mean and standard deviation of the participants' demographic data.
2. Mean values of two independent variables were compared using independent t-test.
3. Sensitivity, specificity, positive predictive value and negative predictive value of elastography are analysed using receiver operating curve (ROC).
4. Agreement between two types of measurement was measured by using The Kappa Statistic with 95% confidence interval

DATA COLLECTION SHEET

DEMOGRAPHIC DATA **Date:**

Name: **Hp No:**
IC No:
Registration No:

1. **Age :_____**
2. **Race: Malay / Chinese / Indian / Others: _____________**
3. **Menopausal status:__________**
4. **Presentation:_____________________________________**
5. **Surgery (particularly to the ipsilateral breast): (yes /no)**
6. **Family history of breast carcinoma: __________________**
7. **Other risk factor:__________________________________**

Table 1: Conventional Ultrasound of solid breast lesion

Location	
Size / measurement (MacMahon *et al.*)	
Margin	**Well / Ill-defined**
Lobulation	**Not present/ Present (macro/microlobulated)**
Echogenicity	**Homogenous / heterogenous**
Calcification	**No / Yes**
Posterior shadowing/ enhancement	**No / Yes**
Axillary nodes	**No / Yes : Benign / Malignant**
Other comment	
BIRADS	

Table 2: Shearwave elastography breast lesion

		Mean (kPa) lesion
Max Elasticity 1	**Max elasticity 2**	
Mean Elasticity 1	**Mean Elasticity 2**	

HPE Results:________________________________

Taken by: FNAC / Biopsy / Surgery **Date: _________________**

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1 INTRODUCTION

Breast cancer is the most common cancer among Malaysian women. There is a marked geographical difference in the worldwide incidence of breast cancer, with a higher incidence in developed countries compared to developing countries.There were 3,242 female breast cancer cases diagnosed in 2007 and reported to NCR (National cancer registry) of Malaysia, accounted for 32.1% of all female cases (Zainal Ariffin and Nor Saleha, 2011). Therefore, screening for early detection of breast cancer is crucial and has become a big challenge in medical field.

Greyscale ultrasound has a long-established role in the assessment of symptomatic breast masses. A sonographic BI-RADS lexicon was used to provide standardized terminology to facilitate accurate and consistent breast sonography and mammography reporting as well as a widely accepted risk assessment. The sonographic BI-RADS descriptors of malignancy include spiculated margin, irregular shape, and nonparallel orientation whereas circumscribed margin, oval shape, and parallel orientation were descriptors for benign lesion. The sonographic BI-RADS lexicon showed 71.3% accuracy, 98.1% sensitivity, 32.9% specificity, 67.8% PPV, and 92.3% NPV. The NPV for class 3 was 92.3%. The PPVs for classes 4 and 5 were 46.6% and 87.3% (Costantini *et al.*, 2006). It is a valuable adjunct to mammography as it is non-invasive and non-radiation tools examination. However, it is known to suffer from unavoidable limitation of low specificity (Corsetti *et al.*, 2006).

In the last 10 years, different sonographic methods have been developed to determine the sonographic features of benign and malignant breast lesion in order to increase the sensitivity in detecting malignant breast lesion. This includes the most recent advancement in assessment of tissue elasticity.

Generally, breast cancer tissue is harder than the adjacent normal breast tissue. This property was the basis for some examinations that are being used in the clinical assessment of breast abnormalities, such as palpation as well as for ultrasound elastography assessment. A study by Itoh *et al.* (2006) shown that ultrasound elastography has nearly the same diagnostic performance as greyscale ultrasound, with 86.5% sensitivity, 89.8% specificity, and 88.3% accuracy in the differentiation of benign from malignant solid breast lesions. However, ultrasound elastography with freehand compression has several disadvantages as it is highly dependent on the surrounding mechanical properties resulting in a substantial amount of interobserver variability during data acquisition and interpretation (Regner *et al.*, 2006). In addition, it only provides qualitative measurement of the tissue elasticity rather than quantitative value.

To overcome this problem, the quantitative elastography technique of shearwave elastography (SWE) has been developed for the past couple of years. SWE allows qualitative as well as quantitative assessment of breast lesions. Unlike conventional or strain elastography methods, which rely on manual compression and measure tissue displacement, SWE does not require manual compression and computes true tissue elasticity by measuring the velocity of shear waves as they propagate in tissue. The system itself induces mechanical vibrations by using an acoustic radiation force created by a focused ultrasound beam. A very fast (5000 frames/s) ultrasound acquisition sequence is used to capture the propagation of the shearwaves. The displacement induced in a breast lesion creates a shearwave that provides information about the local elasticity properties of the tissue and enabling the production of a two-dimensional map of shear elasticity which can be quantify in kilopascal (kPa) (Bercoff *et al.*, 2004; Fink and Tanter, 2010).

The technique was highly reproducible; the intraclass correlation coefficient was 0.8, indicating moderated agreement (Evans *et al.*, 2010). Therefore, SWE could be a valuable adjunct tool in differentiating benign and malignant breast lesions. Within a given region-of-interest (ROI), a variety of stiffness parameters can be measured, including the mean stiffness (Emean), maximum stiffness (Emax), and standard deviation (SD). There were few earlier studies that used different cut-off value (COV) to determine benign and malignant breast lesion. A study by Evans *et al.* (2010) used the COV which was taken from the mean elasticity value of 50kPa. Whereas Chang *et al.* (2011b) used the COV of maximum elasticity of as 80kPa. At this COV, the SWE has sensitivity and specificity of 88.8% and 84.9% respectively.

Since stiffness is a continuous variable, different COV could be chosen. For example, if improved specificity was desired, a higher COV could be used but the cost would be a reduction in sensitivity. Therefore we hope to determine the optimum COV of maximum elasticity for breast cancer in our local population as well as the sensitivity and specificity of SWE for solid breast lesion. This study would have a great impact and benefit to the society as the addition of SWE in ultrasound breast examination might help to differentiate between benign and malignant masses. This may in turn allow a larger proportion of women with benign masses to be reassured and to reduce the number of women subjected to biopsy or short-term follow-up for benign-appearing solid breast lesions.

The general objective of this study was to determine the correlation of SWE solid breast lesions with histopathological findings. The specific objective of this study were (1) to determine the mean of maximum elasticity value of malignant and benign breast lesions (2) to determine the sensitivity and specificity of shear wave elastography correlating with histopathological findings (3) to determine the agreement between SWE and BI-RADS scoring differentiating malignant and benign breast lesions.

2 METHODOLOGY

2.1 Patients

This was a cross sectional study which was conducted in Women's Imaging Suite (WISH) ultrasound room, Hospital Universiti Sains Malaysia from November 2014 until September 2015. This study was approved by Human Research Ethics Committee, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan. Written informed consent was signed and obtained from all patients before the examination and biopsy procedures.

The participants of the study were women with solid breast lesion who came for breast ultrasound examination at our department. The inclusion criteria for our samples recruitment were adult female (more than 18 years old) with solid breast lesion and the histopathological results were available as a gold standard reference. We excluded patient who recently had operation on the ipsilateral breast and those with no histopathology examination result. A total of 224 participants were successfully recruited into this study. However, data from 174 patients were finally analysed as 50 patients were excluded from the study; for non-solid lesion (23) and incomplete of histopathological results (27).

We used Aixplorer® ultrasound system (SuperSonic Imagine, Aix en Provence, France) equipped with a 15-4 MHz linear-array transducer. This system has allowed both greyscale ultrasound as well as SWE assessment in the same setting. The SuperSonic Imagine applications specialist was present at the beginning of the study for practitioner training.

Each patient underwent a conventional greyscale ultrasonography of both breasts followed by SWE. Prior to the ultrasound examination, several demographic data such as age, family history of breast cancer, menopausal status and parity were taken and recorded. Images were recorded in Picture Archiving Computer System (PACS) for retrieval and greyscale ultrasound images were classified according to the American College of Radiology

(ACR) Breast Imaging Reporting and Data System (BI-RADS). BI-RADS categories 1-3 were taken as benign while BI-RADS categories 4-6 were classified as malignant. The combined greyscale ultrasound and SWE examination time was between 10 and 20 minutes. Acquisition of the SWE images added 3 to 5 minutes to the appointment time.

2.2 Greyscale ultrasound and shearwave elastography examination

Both breasts ultrasound examinations were performed first using greyscale ultrasound, locating the solid breast lesion by the researcher and validated by a senior consultant radiologist with 11 years of working experience and subspecialty in breast imaging. Assessment of the breast lesions on greyscale ultrasound were made according to WHO protocol; two orthogonal images for each lesion to evaluate the margin, echopattern, posterior shadowing, calcification and measurements were taken in both transverse and sagittal planes. Final assessments based on greyscale ultrasound features were recorded according to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS).

Following greyscale ultrasound, the SWE images were obtained. Two SWE images were taken for each lesion. The probe was held still over the lesion for about 10 second to allow the shearwave image to build up. Images of greyscale ultrasound and SWE were simultaneously displayed in a split-screen mode with the semi-transparent SWE image superimposed on the corresponding greyscale ultrasound image. The region-of interest (ROI) box of the SWE colour map was set to include the mass and surrounding breast parenchyma tissue sufficiently (Figure 1). During image acquisition, no pressure was applied through the transducer to prevent artefactual stiffness from being recorded. Qualitative elasticity was displayed as a colour map in which the red colour represents a stiff lesion whereas the blue colour represents a soft lesion. The quantitative elasticity values were obtained by moving a