The Role of Strain Elastography in Differentiation Between Metastatic and Benign Axillary Lymph Nodes in Patients with Breast Cancer

Mohammed abd kadhim [*], Donia Abdul-Karim Abdul-Hussein Aljashaami, Noor Kathem Nee'ma Al-Waely*****

ABSTRACT:

BACKGROUND:

Elastography is a promising diagnostic tool that is increasingly used by radiologists to increase the sensitivity and specificity of conventional ultrasound in a wide range of disease processes. One of its major uses was to differentiate between benign and malignant lesions.

OBJECTIVE:

Is to investigate the value of elastography in assessing lymph nodes in the patients with breast carcinoma.

PATIENTS AND METHODS:

This single center prospective cross sectional study involved forty-nine (49) women with breast cancer and the total of sixty (60) lymph nodes (LNs) that were suspicions to be metastatic. The study was carried out at Al-Imamain Al- Kadhimain Medical city/the breast clinic, from January 2016 through October 2016. Ultrasound examination included conventional B-mode, power Doppler and elastography at same session. The results were compared with tissue diagnosis of biopsy specimens and fine needle aspiration cytology.

RESULT:

Our final result included 60 LNs, 33 reactive and 27 metastatic. The Mean of B-mode score of lymph nodes involved by metastasis was higher than that of reactive lymph nodes, 3.26 ±0.98 versus 1.00 ±1.12, and the difference was highly significant ($P<0.001$). While the mean for strain elasticity score of lymph nodes involved by metastasis was higher than that of reactive lymph nodes, 3.89 ±0.70 versus 1.85 ±0.76, and the difference was highly significant ($P<0.001$). The Mean strain ratio of lymph nodes involved by metastasis was higher than that of reactive lymph nodes, 5.04 ±1.96 versus 1.7 ±0.87, and the difference was highly significant ($P<0.001$). Overall sensitivity and specificity of B mode US was 81.5% and 90.9% respectively, sonographic elastography sensitivity and specificity 77.8% and 100.0% respectively, while the sensitivity of combined B mode and elastographic ultrasonography increase to 96.3%.

CONCLUSION:

The present study showed that combined ultrasound B-mode and elastography added significantly to the sensitivity of ultrasound differentiation among benign lymph nodes and those which are involved by malignant metastasis.

KEY WORDS: elastography, breast cancer, axillary lymph nodes.

INTRODUCTION:

Breast cancer is by far the most commonly diagnosed cancer in female worldwide and rank only second to lung cancer as the commonest cause of cancer in both sexes. In the year 2012 about 1.67 million newly diagnosed cases of breast cancer worldwide which represent about 25% of all cancers detected and it ranks fifth as an overall cancer death [(1)]. In Iraq, the incidence is not different and breast cancer account for about one third of all female cancer cases and the incidence rate was increase from 26.6 per 100000 in the year 2000 to affect 31.5 per 100000 in the year 2009. [(2)]

*Professor in Medical Collage/ Al-Nahrain University. Consultant radiologist in Al-Imamian Al-Kadhimyian Medical City.

**Radiologist in Al-Imamian Al-Kadhimyian Medical City.

***Lecturer at Medical College /Al-Nahrain University.
Senior Radiologist at Al-Imamain Al-Kadimyian Medical City.

The most reliable prognostic indicators of disease recurrence and the 5-years survival of patient with breast cancer are significantly affected by the metastatic involvement of axillary LN [3,4]. For pathologic staging of the ipsilateral axillary lymph nodes metastasis, the nodes are classified as pN1, pN2, or pN3, in which pN1 means the presence of one to three metastatic axillary LN; pN2, four to nine metastatic axillary LN; and pN3, 10 or more metastatic lymph nodes. The differentiation between pN1 and pN2 or higher disease is important in decision of further management because locally advanced breast cancer generally needs adequate adjuvant treatment [5].Lymph node (LN) enlargement can be caused by many benign causes like infections and connective tissue disorders or malignant causes including involvement by lymphoma and lymphatic metastasis from primary cancers [6]. Traditionally, surgical axillary lymph node dissection (ALND) has been the method of choice for obtaining histologic information on axillary node status. The removal of axillary LNs also improves overall patient survival [7,8]. However, ALND is the standard method for obtaining lymph node histology, but they found that axillary lymph nodes metastasis is present in only 41% of patients with early breast cancer underwent ALND [9]. The remaining patients are exposed to unnecessary complications like lymphedema, shoulder weakness, arm pain, stiffness, seroma formation, vascular and brachial plexus injuries without any therapeutic benefit[10].

Conventional Ultrasound is the imaging technique most commonly used in clinical practice over the last 45 years because it is easy, available, bed side, real-time imaging, noninvasive, portable, no radiation hazard and low cost [11]. Conventional Ultrasound detection of LNs metastasis depending on following criteria the size, shape, hilum and the abnormal cortical thickness [12]. One of disadvantages is the lack of quantitative properties of tissue elasticity, so surgeon depends on manual palpation for assessment of tissue elasticity [13]. During the latter three decades, a newly developed imaging technique (elastography) that used to assess tissue elasticity that add a lot of information to manual palpation [14]. Elastography is a noninvasive method of imaging stiffness of tissues by quantitative assessment of tissue deformation in response to an applied pressure. It is a method of “virtual palpation” of tissue or lesions, which has the potential to overcome the bias associated with clinical palpation. It can also provide objective and quantitative measures of tissue stiffness [13]. Sonographic elastography when combined with B-mode improve the role of ultrasound in differentiating reactive from metastatic axillary lymph nodes in patient with breast cancer [15].

AIM OF THE STUDY:

To study the value of elastography in assessing malignant lymph nodes in patients with breast cancer.

PATIENT AND METHODS:

This study was conducted at Al-Imamain Al-Kadhimain medical city/ Baghdad/ Iraq from January 2016 to October 2016. Forty nine patients were enrolled in this study with a total of 60 lymph nodes. All patients were referred from the breast outpatient clinic with either proved diagnosis of breast cancer by previous histopathological study of their breast mass (20 patients), or patients with suspicious breast mass referred for radiological evaluation before histopathological examination (22 patients), or patients with previous history of breast cancer treated with mastectomy and presented with enlarged axillary Lymph nodes (7 patients 6 with unilateral mastectomy; and one patients with bilateral mastectomy).

Exclusion criteria are patients with clinically suspicious breast mass and histopathological examination proved to be benign pathology, patients with local skin inflammation and edema, patients in whom histopathological results are not available or not conclusive, and patients with recent history of radiotherapy (during the last 6 months following radiotherapy).

All the patients included in this study were subjected to full history (included demographic data including age, marital status, no. of children, breast feeding, previous history of the breast cancer and family history of breast cancer). Full clinical examinations were done including the breast and axilla.

All patients were examined sonographically starting with gray scale ultrasound and the examination was done with the patient lying in the supine position, then elastographic examination was done. The examination was done using high frequency linear probe (7- 11 MHZ) using Voluson E6 ultrasound machine (GE healthcare, USA). All examinations were documented using clips and selected pictures for further re-evaluation. All the lymph nodes were first examined by gray scale B mode sonography with the patient lying in the supine position and the ipsilateral arm is elevated on the head. All lymph nodes were assessed by 4 criteria: short axis diameter, short to long axis ratio, integrity of the hilum, and the shape of cortex, then according to these findings scoring was done for B mode as follow: short axis (if it is ‹ 10 mm score 0, ≥10mm score 1), short to long axis (‹0.5 score 0, ≥0.5 score 1), presence of hilum or not (if present score 0, absent score 1), cortical thickening (thin cortex score 0, any cortical thickening score 1). All of the above measurements were repeated 3 times and the average was taken.

All lymph nodes were evaluated using color and spectral wave Doppler ultrasound. The results were scored into 2 types: type 1: blood flow either absent or limited to the hilum (score 0), type 2: peripheral (parenchymal) blood flow was seen (score 1).

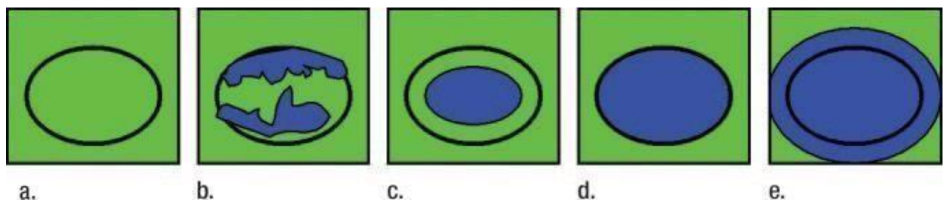

Figure1: elastography score according to *Itoh et al* in which a.ES 1, b.ES 2, c.ES 3, d.ES 4, e.ES 5. the dark line around the lesions represent separation between them and surrounding tissue [21].

Elastographic ultrasonography examination was done with the patient in the same position, elastography was done using real time free hand elastography, the probe applied perpendicular to the skin with light alternating repeated hand compression and decompression until quality control bar on screen corner become green (means satisfactory image). The field of view (FOV) for elastography was adjusted so that the Lymph node is located in its center and not exceed 1/3 FOV with adequate surrounding fat and avoiding bone and blood vessels which affect the analysis of relative hardness of targeted lymph nodes. Using 2 panel images to compare the elastography with real time B mode images. The elastography image then displayed with elasticity color map superimposed on grey image display on left side of dual display image, with B mode image display on right side to maintain real time examination for both modes, then the size of the examined LN was measured in both images (elastography and B mode) and the difference in size was documented, then the elastography color score is determined and documented (from 1 to 5 score), In our work we use the 5 points score used by *Itoh et al* [21] because we found 4 Lymph node with extension outside the B mode margin in elastography (Lymph node appear larger in elastography than in B mode) which represent elastography score (extra nodal extension of malignancy) as shown in figure 1. After that measurement of the strain ratio by using fat tissue at approximately the same level of lymph node as the reference area (ROI area is positioned in the fat and another ROI area is the affected LN and the ratio then calculated automatically). All of the above measurements were repeated 3 times and the average was taken. Histopathological examinations of all the LNs were done (histopathological biopsy for 25 (41.6%) LNs and FNAC for 35 (58.4%) LNs).

Statistical analysis: Data were summarized, analyzed and presented using statistical package for social sciences (SPSS version 22), and Microsoft Office Excel 2013. Numeric (quantitative) variables were expressed as mean, standard deviation and range, whereas categorical (qualitative) variables were expressed as number and percentage. Receiver operator characteristic (ROC) analysis using MedCalc for Windows, version 14.12.0 (MedCalc Software, Ostend, Belgium) was carried out to predict best cut off value for strain ratio and short axis that segregate lymph nodes into benign and malignant. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy was measured for each method alone and then for combined methods. Mann Whitney U test was used to compare median B mode and elasticity score between reactive lymph nodes and those involved by metastasis. P- Value was considered significant when it was less than or equal to 0.05.

RESULTS:

The present study included 60 lymph nodes taken from 49 patients with breast cancer. Their mean age was 50.15 ± 13.47 years and an age range of 26 to

85 years, 18 (34.7 %) patients had right sided lesions whereas 32 (65.3%) patients had left sided lesions.

Mean B-mode score of lymph nodes involved by metastasis was higher than that of reactive lymph nodes, 3.26 ±0.98 versus 1.00 ±1.12, and the difference was highly significant (P<0.001). Distribution of lymph nodes according to individual scores was: in score 0 there are 16 out of 60 LNs (15 LNs are benign according to tissue diagnosis and only 1 LN proved to be metastatic), in score 1 there are 7 out of 60 LNs all of them are benign according to tissue diagnosis, in score 2 there are 12 out of 60 LNs (8 LNs are benign according to tissue diagnosis and 4 LNs proved to be metastatic), in score 3 there are 10 out of 60 LNs (2 LNs are benign according to tissue diagnosis and 8 LNs proved to be metastatic), and in n score 4 there are 15 out of 60 LNs (only 1 LN is benign according to tissue diagnosis and the remaining 14 LNs proved to be metastatic), as shown in table 1.

Mean elasticity score of lymph nodes involved by metastasis was higher than that of reactive lymph nodes, 3.89 ±0.70 versus 1.85 ±0.76, and the difference was highly significant (P<0.001). in ES 1 there are 12 out of 60 LNs all of them are benign according to tissue diagnosis. In score 2 there are 15 out of 60 LNs (14 LNs are benign according to tissue diagnosis, and only 1 LN proved to be metastatic). In score 3 there are 12 out of 60 LNs (7 LNs are benign according to tissue diagnosis and 5 LNs proved to be metastatic). In score 4 there are 17 out of 60 LNs all are metastatic according to tissue diagnosis. In score 5 there are 4 out of 60 LNs all are metastatic according to tissue diagnosis. The Distribution of lymph nodes according to individual elasticity scores is shown in table 1.

Table 1: Mean score and classification of lymph nodes according to each score for both ultrasound B mode and elasticity examination.

Score	Reactive LN (Total No.=33)		Metastatic LN (total No. = 27)		Total	P value
	No.	%	No.	%		
B mode						
0	15	93.8	1	6.3	16	<0.001
1	7	100.0	0	0.0	7	0.011
2	8	66.7	4	33.3	12	0.364
3	2	20.0	8	80.0	10	<0.001
4	1	6.7	14	93.3	15	<0.001
Mean ±SD	1.00 ±1.12		3.26 ±0.98			<0.001*
Elasticity						
1	12	100.0	0	0.0	12	<0.001
2	14	93.3	1	6.7	15	0.001
3	7	58.3	5	41.7	12	0.795
4	0	0.0	17	100.0	17	<0.001
5	0	0.0	4	100.0	4	0.022
Mean ±SD	1.85 ±0.76		3.89 ±0.70			<0.001*

*Highly significant according to Mann Whitney U test (significant P value ≤ 0.05)

Mean strain ratio of lymph nodes involved by metastasis was higher than that of reactive lymph nodes, 5.04 ±1.96 versus 1.7 ±0.87, and the difference was highly significant (P<0.001). Distribution of lymph nodes according to individual strain ratio intervals is shown in table 2.

Table 2: Classification of lymph nodes according to Strain ratio.

Strain Ratio Interval	Reactive LN (No.)	Metastatic LN (No.)	Total
0.3-1.3	13	1	14
>1.3-2.3	13	1	14
>2.3-3.3	5	5	10
>3.3-4.3	2	1	3
>4.3-5.3	0	7	7
>5.3-6.3	0	6	6
>6.3	0	6	6
Total	33	27	60
Mean ±SD	1.7 ±0.87	5.04 ±1.96*	

* P<0.001 according to Mann Whitny U test

The B mode Ultrasound: the sensitivity of short axis alone was 59.35 with a specificity of 87.9 and overall accuracy rate of 81.9 %, whereas the sensitivity of Short to long axis ratio (S/L) gave better sensitivity of 85.2 % with less specificity of 78.8 % and a comparable overall accuracy of 81.7 %. Presence versus absence of hilum brought about same values of the sensitivity, specificity and accuracy of Short to long axis ratio. Abnormal cortical thickening yielded a sensitivity of 85.2%, a specificity of 72.7 % and overall accuracy rate of 78.3%. Each individual score of B-mode has been analyzed and the results concerning sensitivity are shown in table 3. The best B-mode score regarding both sensitivity and specificity was score 2/3. Power Doppler gave an excellent sensitivity of 92.6 %, a very good specificity of 81.8% and an overall accuracy rate of 86.7 %, as shown in table 3.

Elasticity score and strain ratio: the sensitivity, Specificity, PPV, NPV and Accuracy of each elasticity score is shown in table 3. Score 1 and 2 show sensitivity 100% and specificity 36.4% The most accurate score was 3/4 with a sensitivity of 77.8%, a specificity of 100% and accuracy rate of 90 %.

The sensitivity, Specificity, PPV, NPV and Accuracy of each strain ratio score is also shown in table 3. The most accurate strain ratio was >3.4 with a sensitivity of 74.1%, a specificity of 97% and accuracy rate of 86.7 %.

Table 3: Sensitivity of B- mode and power doppler ultrasound and elasticity score in differentiation between reactive and metastatic LNs.

Parameter	Sensitivity	Specificity	PPV	VPV	Accuracy
Short axis diameter (10.5)	59.3	87.9	80.0	72.5	81.9
S/L ratio (0.6)	85.2	78.8	76.7	86.7	81.7
Hilum	85.2	78.8	76.7	86.7	81.7
Cortical thick	85.2	72.7	71.9	85.7	78.3
B mode					
0/1	96.3	45.5	59.1	93.8	68.3
½	96.3	66.7	70.3	95.7	80.0
2/3	81.5	90.9	88.0	85.7	86.7
¾	51.9	96.9	93.3	70.5	76.3
Power Doppler	92.6	81.8	80.6	93.1	86.7
Elasticity score					
½	100.0	36.4	56.3	100.0	65.0
2/3	96.3	36.4	55.3	92.3	63.3
¾	77.8	100.0	100.0	84.6	90.0
4/5	14.8	100.0	100.0	58.9	61.7
Strain ratio					
> 1.3	96.3	39.4	56.5	92.9	65.0
> 1.9	96.3	69.7	72.2	95.8	81.7
> 2.5	85.2	81.8	79.3	87.1	83.3
> 3.4	74.1	97.0	95.2	82.1	86.7
> 4	70.4	100.0	100.0	80.5	86.7

- PPV=positive predictive value, NPV=negative predictive value

Diagnostic performance of elasticity score and strain ratio were analyzed using receiver operator characteristic (ROC) curve analysis (figure 2) which give the cut off value of elasticity score and strain ratio with best sensitivity and specificity for differentiating metastatic from benign axillary lymph nodes and results are shown in table 4.

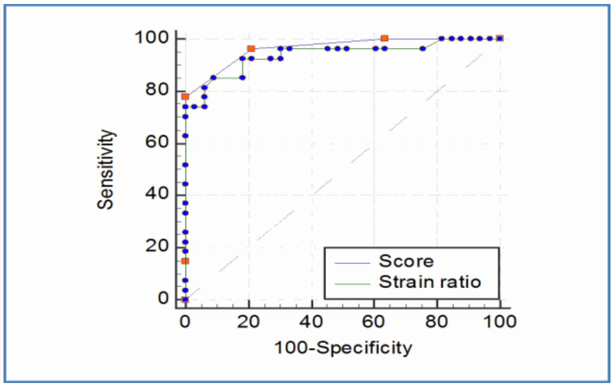

Figure 2: Receiver operator characteristic (ROC) curve analysis for identification of cut off value of elasticity score and strain ratio

Table 4: Values obtained by ROC analysis.

Parameter	Cut off value	Sensitivity	Specificity	AUC*	P value
Elasticity score	¾	77.8	100.0	0.965	<0.001
Strain ratio	> 3.4	74.1	97.0	0.939	<0.001

*AUC area under curve.

Results of combined B-mode and elastographic ultrasonography: the sensitivity of combined methods, B-mode and elastographic ultrasonography, was 96.3 which is far better than individual methods. Specificity was less; moreover, the overall accuracy of combined methods was less than that of each individual method, 85.0% versus 86.7% and 90.0% as shown in table 5.

Table 5: The results of combined B-mode and elastographic ultrasonography.

Method	Sensitivity	Specificity	PPV	NVP	Accuracy
B-mode	81.5	90.9	88.0	85.7	86.7
Elastography	77.8	100.0	100.	84.6	90.0
Combined	96.3	75.8	76.5	96.2	85.0

Figures 3 and 4 show some cases from the study.

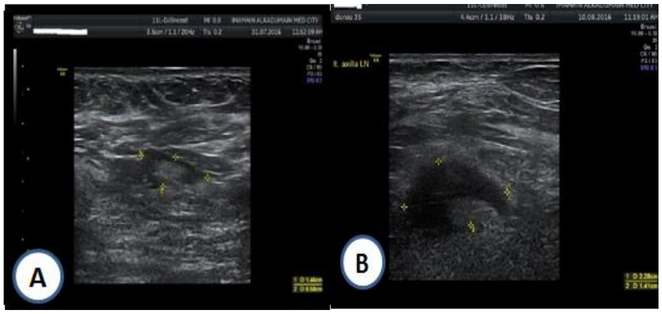

Figure 3: A: 40 years old female with axillary LN, B mode score 0: short axis less than 10 mm (0), Short/Long axis ratio more less than 0.5 (0), hilum present (0), thin cortex, (0) biopsy proved it benign. B: Show LN in 40 nyears old female with B mode score 3: short axis more than 10 mm (1), S/L axis is more 0.5 (1),preserved hilum (0), abnormal cortex (1), biopsy proved involvement by metastasis.

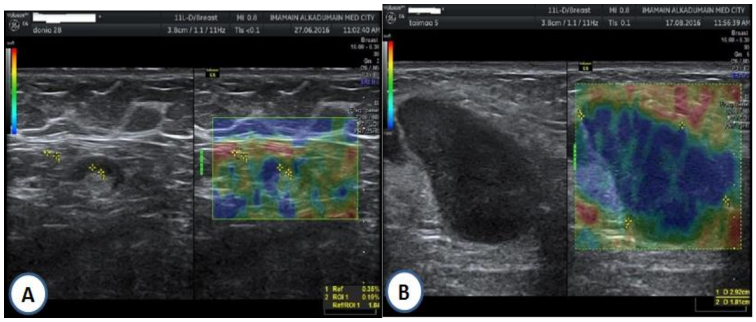

Figure 4 Show axillary LN in 43 eyears old female with elastography score 1 and strain ratio 1.8 biopsy prove it benign. B: Show axillary LN in 45 years old female with elastography score 4 biopsy prove metastatic involvement.

DISCUSSION:

Ultrasonography is the routine test for the preoperative assessment of axillary lymph nodes in patient with breast cancer, with a sensitivity ranging from (35%-95%) depending on the skills of the operator and the parameters used as a predictor for metastatic involvement [16]. In this study the data obtained by using B mode score are approximately similar to that used by *Choi et al* [12] with slight difference: our cut off value of Short axis was 10.5 mm, and we used Short to Long axis value instead of Long to Short axis (L/S) value which gives us highest sensitivity and specificity, presence or absence of fatty hilum and abnormal cortical thickening, all these criteria produce 5 point scoring for B mode (starting from 0 to 4). In our result the presence or absence of fatty hilum and short to long axis ratio have highest sensitivity and specificity (85.2% and 78.8% respectively), this showed slight difference from that of *Choi et al* [12] and this could be attributed to the use of 7mm the cut of value for short axis in their study, with a sensitivity of 74.2% and 90% specificity, on the other hand there is general agreement regarding the significant difference of distribution of benign and metastatic lymph nodes between different B mode scores as follow: 74.2% of metastatic nodes (23 of 31) showed B mode scores of 2 to 4 while our results show 96.3% (26 of 27), and 78.8% of reactive lymph nodes (26 of 33) showed B-mode scores of 0 and 1 (while our results show 66.7%, 22 of 33). Abe et al (17) found the overall sensitivity and specificity of preoperative axillary LN ultrasonography (75%, and 88% respectively). In this study the US finding of absence of hilum had the highest predictive value followed by cortical thickening combined with non-hilar cortical blood flow, with a PPV of 81%, while *Sousa et al.* [18] reported a 100% positive predictive value on finding of cortical thickness and non-hilar cortical vascular flow, while our results showed (92.6%, 81.8% and 80.6) for sensitivity, specificity and PPV which is near the results of *Abe et al* [17]. Another study done by Oz et al [19] used the same criteria that used in our study, (cortical thickening >3 mm, increase the size of lymph node, an increase in short to long diameter, increased cortical hypo echogenicity, and non-hilar cortical flow) and reported a sensitivity and specificity of 88.5% (versus 81.5%) and 100%(versus 90.9%), respectively, and positive predictive value of 100% (versus 88%) and negative predictive value of 66.6% (versus 85.7%). Taylor et al [20] (work on axillary LN in 50 patients with breast cancer) described a sensitivity and specificity of 76% and78% for conventional ultrasound. *Kaur et al* [12] also used all the criteria we used in the B mode evaluation of axillary LN with the same cut off point for short axis (10 mm) with sensitivity and specificity (81.8% and 16.6% respectively) versus (59.3% and 87.9% in our study), while regarding loss of hilum they found 70.4%, 83.3% and 91.6% (vs. 85.2%, 78.8% and 76.7%) for sensitivity, specificity, and positive predictive value respectively. For abnormal cortical thickness their result report (50%, 44.4% and 54.4%) (vs. 85.2%,72.7% and 71.9%) for sensitivity, specificity, and positive predictive value respectively. For abnormal shape (S/L) value their results were 63.6%, 77.7% and 87.5% (vs. 85.2%, 78.8% and 76.7%) for sensitivity, specificity, and positive predictive value respectively. *Wojcinski et al* [22] use the B-Mode-US for evaluation of 180 axillary LN with criteria of cortex >3mm (sensitivity 40% and specificity 96.8%) and Doppler-US (sensitivity 14.3% and specificity 95.6%). From the results of the previously mentioned studies regarding the use of B mode sonography in the evaluation of axillary LN, there is a wide range of variations between the studies, so it is important that these results to be supported by elastography.

Elastography: in the current study we use 5 point scoring system based on Elastography score system reported by Itoh et al [23]. This scoring system used also by *Alam et al* [24], and *Ishibashi et al* [25] in their works on cervical lymph nodes, which was modified by *Choi et al* [12], *Furukawa et al* [26,27] and *Lyshchik et al* [28] in their works on axillary and cervical lymph nodes, respectively, to 4 points score and explained this modification because no necrotic axillary lymph nodes were included in his study. Our results suggested that there was a significant difference in elasticity scores between reactive and metastatic axillary lymph nodes, it had been found that 77.8% of metastatic nodes (21of 33) had an elasticity score of 4 and 5, and 78.8% of reactive nodes (22 of 33) had an elasticity score of 1 or 2, while score 3 has no significant differentiating value between metastatic and reactive lymph node (7 of 33 (21.2%) reactive and 5 of 27 (18.5%) metastatic. So elastography score 3/4 had a sensitivity 77.8% and specificity 100%. Wojcinski et al [29] used a simple 5 points color scale work on axillary lymph nodes in breast cancer describing the predominant color of the distinct structure (red, yellow, green, turquoise, or blue) as it appears in the elastogram (sensitivity 60% and specificity 79.6%). Another similar study by *Giovannini et al*. [29] showed high sensitivity (100%) but the specificity is 50%. *Choi et al*. ([12] used the modified 4 points scoring system and classified 64 axillary LNs using a 4-point color scale based on the percentage and distribution of the LN areas with high elasticity (in which blue color mean hard). They achieved sensitivity of 80.7% and specificity of 66.7% and optimal cut off value between score 2 and 3. *Alam et al*. [24] studied the role of elastography on cervical LNs in 85 patients. They used 5 points scoring system according to the distribution and percentage of the LN area with high elasticity (i.e. hard, blue), with pattern 1 being an absent or very small hard area and pattern 5 indicating a hard area occupying the entire LN. The cutoff line for reactive versus metastatic was set between patterns 2 and 3. The authors reported sensitivity of 83% and specificity of100%.Taylor et al. [20] used sonoelastography in 50 patients with breast cancer. They evaluated the axillary LNs in the elastogram using either an individual visual scoring system or an individual strain scoring system. They reported sensitivity and specificity 90% and 86% for visual scoring, and 100% and 48% for strain scoring, respectively.

Combined B mode and elastographic ultrasound: by using combined (B mode and elastographic ultrasonography) sensitivity had reached 96.3% compared to that of B mode and elastography separately (81.5%, 77.8% respectively), but there was decrease in specificity. These results were in concordance with that of *Choi et al* [12] which showed similar increase in sensitivity and decrease in specificity. While *Young et al* (30)who studies axillary LN show that the accuracy of SE lower than conventional US and add no value when combined with conventional US ,so this disagree with us, this disagreement may be explained by that elastography is an operator dependent ,or they used an old version devices,

Stain ratio: another method for the interpretation of elastogram is the calculation of the strain-ratio using fat as a reference tissue. A few previously reported studies have shown that the strain ratio is useful for differentiating benign and malignant lesions in breast masses, axillary and cervical lymph nodes. [12,15,28]. Our cut off value was 3.4 with sensitivity and specificity (74.1% and 97.0%, respectively), this difference was statistically significant (P value 0.001) with more of reactive LN below this value (31 out of 38 LNs with SR at this range) and metastatic LN above it (20 out of 22 LNs with SR at this range). *Choi et al* [12] studied the strain ratio in the evaluation of axillary LNs using fat as a reference tissue with cut off value was 2.3, the sensitivity, specificity, PPV, NPV, and accuracy were 82.8%, 56.3% 61.5%, 77.3%, and 67.2%, respectively. *Lyshchik et al* [28] studied the strain ratio in the cervical LNs but they used the muscle as a reference tissue, so their cut off value was >1.5 with sensitivity, specificity, PPV and NPV were 85%, 98%, 96 % and 90% respectively. The difference in cut off value mostly attributed to the difference in using the reference tissue.

CONCLUSION:

There is significant elastographic difference between reactive and metastatic lymph nodes in the patient with breast cancer. Increased sensitivity of B mode ultrasound in detection of metastasis to lymph nodes when combined with elastography. Measuring strain ratio providing semi quantitative method for detection of metastatic lymph nodes. All these noninvasive methods when used alone or in combination may provide early detection of metastasis and may be used by surgeons for correct planning for surgical options and avoiding the complications of invasive diagnostic methods.

REFERENCES:

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International journal of cancer. 2015;136:E359-86.
2. Al-Hashimi MM, Wang XJ. Breast cancer in Iraq, incidence trends from 2000-2009. Asian Pacific journal of cancer prevention: APJCP. 2013;15:281-86.
3. Liao GS, Chou YC, Hsu HM, et al. The prognostic value of lymph node status among breast cancer subtypes. The American Journal of Surgery. 2015;209:717-24.
4. Dong G, Wang D, Liang X, et al. Factors related to survival rates for breast cancer patients. International journal of clinical and experimental medicine.2014;7:3719.13.
5. Neal CH, Daly CP, Nees AV, et al. Can Preoperative Axillary US Help Exclude N2 and N3 Metastatic Breast Cancer? 1. Radiology. 2010;257:335-41.
6. Chen SJ, Lin CH, Chang CY, et al. Characterizing the major sonographic textural difference between metastatic and common benign lymph nodes using support vector machine with histopathologic correlation. Clinical imaging. 2012;36:353-59.
7. Beenken SW, Urist MM, Zhang Y, et al. Axillary lymph node status, but not tumor size, predicts loco regional recurrence and overall survival after mastectomy for breast cancer. Annals of surgery. 2003 ;237:732-39.
8. Badgwell BD, Povoski SP, Abdessalam SF, et al. Patterns of recurrence after sentinel lymph node biopsy for breast cancer. Annals of surgical oncology. 2003;10:376-80.
9. Mincey BA, Bammer T, Atkinson EJ, et al. Role of axillary node dissection in patients with T1a and T1b breast cancer: Mayo Clinic experience. Archives of Surgery. 2001;136:779- 82.
10. Soares EW, Nagai HM, Bredt LC, et al. Morbidity after conventional dissection of axillary lymph nodes in breast cancer patients. World journal of surgical oncology. 2014;12:1.
11. Gennisson JL, Deffieux T, Fink M, et al. Ultrasound elastography: principles and technique .diagnostic and interventional imaging .2013;94:487-95.
12. Choi JJ, Kang BJ, Kim SH, et al. Role of sonographicelastography in the differential diagnosis of axillary lymph nodes in breast cancer. Journal of Ultrasound in Medicine. 2011;30:429-36.
13. Gupta AK, Chowdhury V, Khandelwal N. Diagnostic Radiology: Recent Advances and Applied Physics in Imaging. JP Medical Ltd; 2013;3:37-54.
14. Sarvazyan A, J Hall T, W Urban M, et al. An overview of elastography-an emerging branch of medical imaging. Current medical imaging reviews. 2011;7:255-82.
15. Cho N, Moon WK, Kim HY, et al. Sonoelastography strain index for differentiation of benign and malignant non palpable breast masses. Journal of Ultrasound in Medicine. 2010;29:1-7.
16. Deurloo EE, Tanis PJ, Gilhuijs KG, et al. Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. European Journal of Cancer. 2003 ;39:1068-73.
17. Abe H, Schmidt RA, Kulkarni K, et al. Axillary lymph nodes suspicious for breast cancer metastasis: sampling with US-guided 14-Gauge Core-Needle Biopsy—Clinical Experience in 100 patients 1. Radiology. 2009;250:41-49.
18. Sousa MT, Illescas MB, Rodríguez MR, et al. Preoperative staging of axillary lymph nodes in breast cancer: ultrasonographic parameters and ultrasound-guided core needle biopsy. Radiología (English Edition).2011;53:544-51.
19. Oz A, Demirkazik FB, Akpinar MG, et al. Efficiency of ultrasound and ultrasound -guided fine needle aspiration cytology in preoperative assessment of axillary lymph node metastases in breast cancer. Journal of breast cancer. 2012;15:211-17.
20. Taylor K, O'Keeffe S, Britton PD, et al. Ultrasound elastography as an adjuvant to conventional ultrasound in the preoperative assessment of axillary lymph nodes in suspected breast cancer: a pilot study. Clinical radiology. 2011;66:1064-71.
21. Kaur N, Sharma P, Garg A, Tandon A. Accuracy of individual descriptors and grading of nodal involvement by axillary ultrasound in patients of breast cancer. International journal of breast cancer. 2013 .

22. Wojcinski S, Dupont J, Schmidt W, et al. Real-time ultrasound elastography in 180 axillary lymph nodes: elasticity distribution in healthy lymph nodes and prediction of breast cancer metastases. BMC medical imaging. 2012;12:1.

23. Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of us elastography for diagnosis 1. Radiology. 2006;239:341-50.

24. Alam F, Naito K, Horiguchi J, et al. Accuracy of sonographicelastography in the differential diagnosis of enlarged cervical lymph nodes: comparison with conventional B-mode sonography. American Journal of Roentgenology. 2008;191:604-10.

25. Ishibashi N, Yamagata K, Sasaki H, et al. Real-time tissue elastography for the diagnosis of lymph node metastasis in oral squamous cell carcinoma. Ultrasound in medicine & biology. 2012;38:389-95.

26. Furukawa MK, Fujita Y, Kubota A, et al. Diagnosis of cervical lymph node metastasis of head and neck squamous cell carcinoma - usefulness of Power Doppler ultrasonography and elastography. Medix 2007; Suppl:20-23.

27. Furukawa MK, Kubota A, Hanamura H, et al. [Clinical application of real-time tissue elastography to head and neck cancer--evaluation of cervical lymph node metastasis with real- time tissue elastography]. Nihon JibiinkokaGakkaiKaiho. 2007;110:503-5.

28. Lyshchik A, Higashi T, Asato R, et al. Cervical Lymph Node Metastases: Diagnosis at Sonoelastography—Initial Experience 1. Radiology. 2007;243:258-67.

29. Giovannini M, Thomas B, Erwan B, et al. Endoscopic ultrasound elastography for evaluation of lymph nodes and pancreatic masses: a multicenter study. World journal of gastroenterology. 2009;15:1587-93.

30. Young Mi Park, Bruno D. Fornage, Ana Paula Benveniste, et al. Strain Elastography of Abnormal Axillary Node in Breast Cancer Patients Does Not Improve Diagnostic Accuracy Compared with Conventional Ultrasound Alone. American Journal of Roentgenology 2014; 203:6.