

Role of Sonoelastography Using 5-Point Scoring Method and Strain Ratio in Improving Diagnostic Performance of Conventional Ultrasound in Indeterminate BI-RADS 3 and 4 Breast Lesions

AHMED M. MAGDY, M.D.*; MENNA ALLAH S. MOHAMED, M.Sc.* and DINA H. GAMAL EL-DIN, M.D.**

The Department of Radiodiagnosis, Faculties of Medicine, Fayoum and Cairo** Universities*

Abstract

Background: Breast cancer is considered the most common cancer worldwide. Finding a non-invasive method that could increase the accuracy of characterization of breast lesions and consequently decrease the unnecessary biopsies of benign lesions is pivotal. Sonoelastography could help in characterization of the indeterminate cases of ultrasound BI-RADS 3 and 4 breast lesions by upgrading or downgrading them.

Aim of Study: To evaluate the usefulness of sonoelastography (using 5-point scoring method and strain ratio) in improving the diagnostic performance of conventional ultrasound in indeterminate cases of US BI-RADS 3 & 4 breast lesions; to guide the diagnostic workup towards biopsy or follow-up.

Patients and Methods: Our study is prospective. 90 female patients were included in our study; who presented with breast lumps and examined by ultrasound and sonoelastography (strain elastography) in the radiology department of our hospital. Initially; conventional breast ultrasonography was performed for the patients and classified according to the ultrasound 'breast imaging, report and data systems' (BI-RADS) categories. Only the patients with ultrasound BI-RADS 3 & 4 category were included in our study. Then strain sonoelastography was performed. Lesions were categorized based on Tsukuba strain scoring system (Elasticity score). Strain ratio (SR) was then calculated for all lesions. We used true cut biopsy, aspiration cytology or excision biopsy for histopathological analysis which was the standard reference.

Results: We found that when a cutoff value of 3.6 was used for the strain ratio: The sensitivity, specificity, PPV, NPV, and accuracy rates were determined as 91.7%, 77.8%, 73.3%, 93.3% and 83.3%, respectively. When the cutoff value of 4 for the elasticity score used; the sensitivity, specificity, PPV, NPV, and accuracy rates were determined as 91.7%, 88.9%, 84.6%, 94.1% and 90% respectively.

Conclusion: Breast strain elastography using 5-point scoring method and strain ratio was found to be of high sensitivity, specificity and diagnostic accuracy in differentiating benign from malignant breast lesions initially categorized as US BI-RADS 3 & 4. It provides additional information on

tissue stiffness to increase the diagnostic performance of conventional ultrasound in the setting of indeterminate BI-RADS 3 and 4 lesions; guiding the diagnostic workup towards biopsy or follow-up and thus reducing the rate of unnecessary biopsies.

Key Words: Breast lesions – Conventional ultrasound – Ultrasound elastography – Strain ratio.

Introduction

ALTHOUGH most breast masses are benign; breast cancer is considered the most common cancer worldwide. Mammography and ultrasonography are the most commonly used screening tests for breast masses [1].

Mammography often yields false negative results in dense breasts. Ultrasound (US) has a high sensitivity in detecting lesions but poor specificity. To improve the specificity; the American College of Radiology (ACR) introduced the Breast Imaging and Reporting Data System (BI-RADS) which is a standardized risk assessment tool used to categorize breast masses [2].

Both mammography and breast ultrasound have some limitations in differentiating benign from malignant lesions; so biopsy is required to reach histopathological diagnosis. That is why; non-invasive method that could increase the accuracy of characterization of breast lesions and consequently decrease the unnecessary biopsies of benign lesions is pivotal [1].

Ultrasound elastography is a technique that applies compression to detect stiffness variation within the examined tissues. Malignant lesions are stiffer than benign ones due to the desmoplastic reaction they contain. Ultrasound elastography (USE) uses this principle to distinguish between malignant and benign breast lesions [3,4].

Correspondence to: Dr. Ahmed M. Magdy, The Department of Radiodiagnosis, Faculty of Medicine, Fayoum University

Strain elastography (SE) evaluates compressibility (elasticity) of the tissues. The elasticity of the targeted breast lesion is compared with that of the normal surrounding subcutaneous fat and is scored from 1 to 5. Since this scoring method is subjective; an index known as “strain ratio” (SR) is defined for semi-quantitative assessment of tissue stiffness. Shear wave elastography (SWE) is a quantitative technique that measures and quantifies the tissue stiffness [5,6,7].

Ultrasound elastography is a promising technique in improving the differentiation of benign from malignant breast lesions [3,8].

Several studies suggested that sonoelastography may be most helpful in characterization of the indeterminate cases of ultrasound BI-RADS 3 and 4 breast lesions by upgrading or downgrading them [9].

Patients and Methods

The aim of our study was to evaluate the usefulness of sonoelastography (using 5-point scoring method and strain ratio) in improving the diagnostic performance of conventional ultrasound in indeterminate cases of US BI-RADS 3 & 4 breast lesions; to guide the diagnostic workup towards biopsy or follow-up.

This study is a single-center prospective study enrolled a total of 90 female patients (mean age was 38.56 ± 14.06 years, range 17-67 years) referred from the general surgery outpatient clinic and presented with breast lump on clinical examination. Our study was conducted between January 2019 and October 2021. The patients were examined by ultrasound and sonoelastography (strain elastography) in the radiology department of our hospital. Only patients with ultrasound BI-RADS 3 & 4 category were included in our study. We used true cut biopsy, aspiration cytology or excision biopsy for histopathological analysis which was the standard reference. The local ethical committee approved this prospective study and written informed consent was taken.

Inclusion criteria:

- Female patients presented with breast lumps on clinical examination.
- Patients with ultrasound BI-RADS 3 & 4 category.
- Patients who consent.

Exclusion criteria:

- Patients with clinical evidence of acute diffuse breast infection and acute abscess.

- Treated breasts (post-operative).
- Breast implants.
- Declined consent.
- Declined biopsy.
- Known histology.

All patients were subjected to:

- Full history taking and examination.
- Conventional ultrasonography and sonoelastography examinations by LOGIQ S8 with XD clear machine equipped with real-time elastography software and a L3-12 linear transducer. Patients were examined in the supine position with the arm placed behind the neck. A 5-10 MHz US linear probe was used.
- Firstly; conventional ultrasound was performed for the patients to assess the breast lesion regarding size, shape, border characteristics, echogenicity, posterior acoustic features, presence of calcification within the lesion and vascularity. The images of these features were recorded and lesions were categorized according to the ultrasound ‘breast imaging, report and data systems’ (BI-RADS) categories. Only patients with ultrasound BI-RADS 3 & 4 category were included in this study.
- Strain sonoelastography was performed instantly after conventional ultrasound. The transducer was placed on the targeted breast mass parallel to long axis of the mass lesion. Then; the sonoelastography box was placed over the mass lesion to be evaluated after acquisition of complete ultrasonography view of the lesion on the screen and performed 4-6 consecutive compression-decompressions in antero-posterior direction.
- Elasticity score (ES): A chromatic scale used to assign soft tissues which could be compressed/strained green color and hard tissues which were not compressible blue color.
- The masses were categorized based on Tsukuba strain scoring system [9,10] where score 1 to 3 are considered benign and score 4 and 5 considered malignant (Fig. 1):
 - Score 1 (predominantly green) is used for lesions which present similar deformability to the surrounding breast parenchyma.
 - Score 2 lesions are those with an inhomogeneous deformability; the overall appearance being a mosaic pattern of green and blue.
 - Score 3 lesions are those with elastic (green) periphery and stiff (blue) core.

- Score 4 lesions are those with no strain in the entire lesion. The entire lesion displayed as blue.
- Score 5 lesions are those with no strain in the entire lesion and the surrounding area. The entire lesion and the surrounding area displayed as blue.

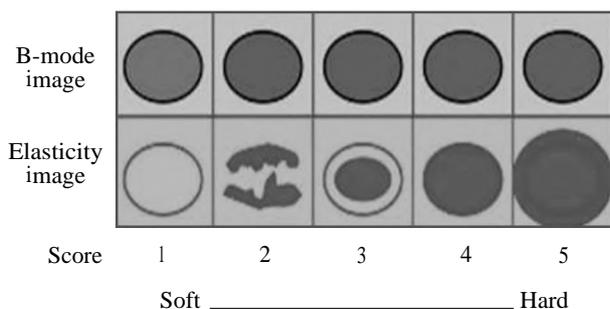


Fig. (1): 5-point color scale (Tsukuba strain scoring system) [10].

- Strain ratio (SR): A target region of interest (ROI) on the breast mass was selected with another one on the adjacent subcutaneous adipose tissue at a similar depth. SR for the breast lesion was then calculated using specific software and SR value was displayed on the image.
- We used true cut biopsy, aspiration cytology or excision biopsy for histopathological analysis which was the standard reference.

Statistical analysis:

The collected data were organized, tabulated and statistically analyzed using SPSS software statistical computer package version 22 (SPSS Inc, USA). The quantitative data were presented by using mean, standard deviation, median, minimum and maximum. The categorical data were presented by frequency (count) and relative frequency (percentage). Standard diagnostic indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic efficacy were calculated. ROC curve was constructed with area under curve analysis performed to detect best cutoff value of SR for differentiating malignant from benign lesions. *p*-value <0.05 was considered statistically significant.

Results

The study included a total of 90 female patients presented with breast lump on clinical examination. Only patients with ultrasound BI-RADS 3 & 4 category were included in our study. The mean patient age was 38.56 ± 14.06 years (range 17-67 years); 54 of them had benign lesions (60%) and 36 had malignant lesions (40%).

30 of the malignant lesions were invasive ductal carcinoma (IDC) (83.3%), 4 were invasive lobular carcinoma (ILC) (11.1%) and two were mucinous carcinoma (5.6%) (Table 1).

Table (1): Types of malignant lesions in our study.

Diagnoses	N	%
IDC	30	83.3
ILC	4	11.1
Mucinous carcinoma	2	5.6
Total	36	100.0

45 of the benign lesions were fibroadenomas (83.3%), 6 were granulomatous mastitis (11.1%) and 3 were chronic abscesses (5.6%) (Table 2).

Table (2): Types of benign lesions in our study.

Diagnoses	N	%
Fibroadenomas	45	83.3
Granulomatous mastitis	6	11.1
Chronic abscesses	3	5.6
Total	54	100.0

ES was significantly higher in malignant breast lesions compared to benign lesions (*p*-value <0.0001).

Table (3): Differences in SR between benign and malignant lesions.

Variable	Mean ± SD Median (range)			<i>p</i> -value
	All patients	Malignant	Benign	
SR	4.59±2.75 3.6 (1-10)	6.43±1.85 6.7 (3-9)	2.37±1.28 2.6 (1-10)	<0.0001*

SR was significantly higher in malignant breast lesions compared to benign lesions (*p*-value <0.0001). The mean value for malignant lesions was (6.43) and that for benign lesions was (2.37). The range of SR for malignant lesions was (3-9) with median value of about (6.7). The range of SR for benign lesions was (1-10) with the median value of about (2.6) (Table 3).

Diagnostic accuracy of ES & SR compared to final pathological diagnosis in distinguishing malignant from benign lesions: The ES shows (91.7%) sensitivity, (88.9%) specificity, positive predictive value of about (84.6%) and negative predictive value of about (94.1 %) with total accuracy of about (90%) when the cutoff point 4 used. The SR shows (91.7%) sensitivity, (77.8%) specificity, positive predictive value of about (73.3%) and negative

predictive value of about (93.3%) with total accuracy of about (83.3%) when the cutoff point 3.60 used; area under curve (AUC) = 0.900, p -value = <0.0001 (Figs. 2,3).

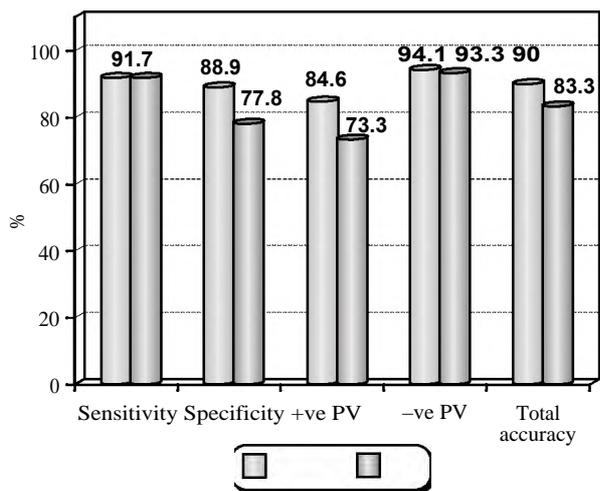


Fig. (2): Diagnostic accuracy of ES & SR compared to final pathological diagnosis in distinguishing malignant from benign lesions.

Breast elastography was found to be of high sensitivity and specificity in differentiating between benign and malignant breast lesions (Figs. 4,5,6).

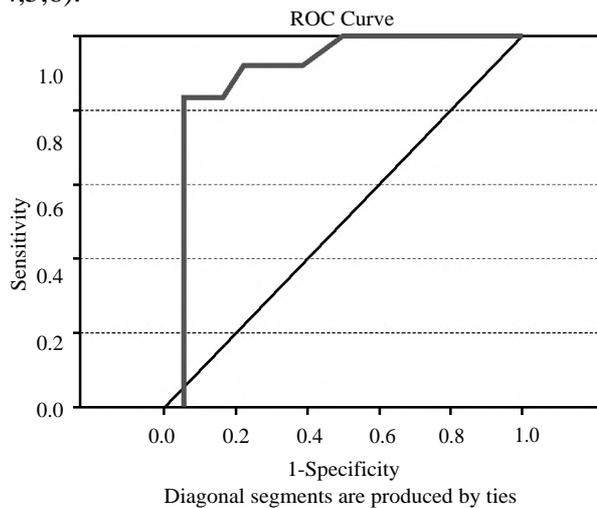


Fig. (3): ROC curve of SR, when the cutoff point of SR=3.60, area under curve (AUC)=0.900, p -value=<0.0001.

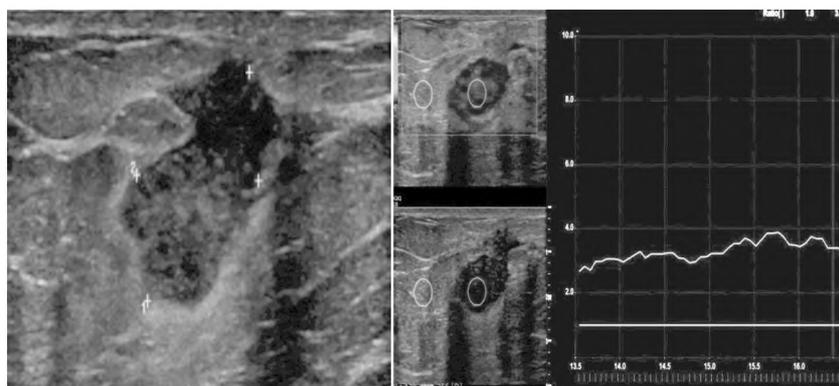


Fig. (4): A 34 year old female patient; gave history of left breast abscess six months ago that was surgically drained. Now she presents with left breast lump. Ultrasound exam revealed an irregular shaped highly turbid fluid collection. The lesion was given (BI-RADS 3) category. Elastography revealed ES of about (1) and SR of about (1.8) denoting that the lesion is benign in nature. Aspiration revealed thick yellowish fluid (chronic abscess).

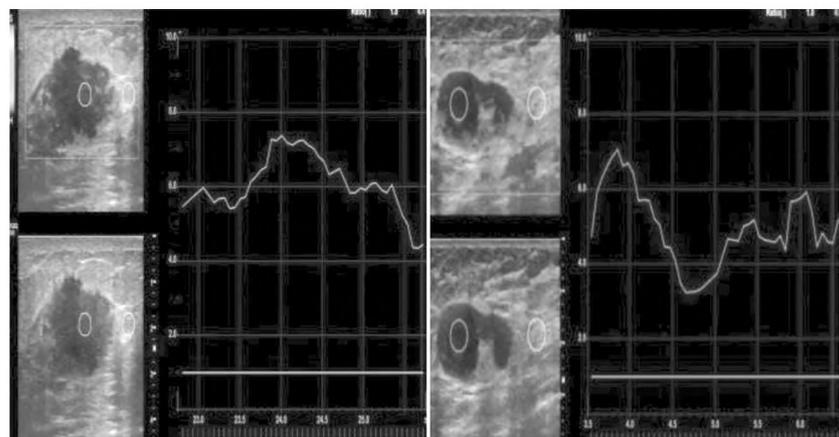


Fig. (5): A 45 year old female patient presented with accidentally discovered right breast lump. (A) Ultrasound shows an irregular shaped hypoechoic soft tissue mass lesion measuring about (34x24 mm). The lesion was given (BI-RADS 4) category. Elastography shows the lesion is stiff (blue on color scale) with ES of about (5) and SR of about (4.4) that favors malignancy. The lesion was pathologically proved to be invasive ductal carcinoma grade II. (B) Companion right axillary lymph node noted that measures about (27x15 mm) showing focal cortical thickening with partially effaced fatty hilum. Elastography revealed elasticity score of about (5) and strain ratio of about (4.6) (i.e. malignant) that was confirmed by pathology. This finding raises the concern for the utility of sonoelastography in lymph nodes characterization.

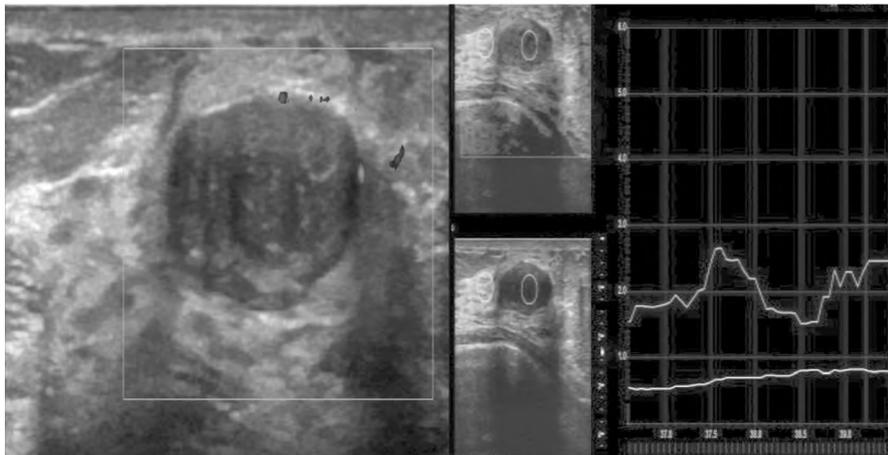


Fig. (6): A 25 year old female patient presented with mobile right breast mass that was accidentally discovered 5 months ago. Ultrasound shows an oval shaped hypoechoic mass lesion with posterior acoustic enhancement measuring about (22x11 mm) that was mobile during examination. Color Doppler shows trivial peripheral vascularity. By conventional ultrasound the lesion was given (BI- RADS 3) category. Elastography shows ES of about (2) and SR of about (2.3) proving the benign nature of the lesion that was pathologically proved to be fibroadenoma.

Discussion

Non-invasive method that could help to increase the sensitivity and specificity of ultrasonography and mammography; thus decreasing unnecessary biopsies of benign breast lesions is required [1].

The aim of our study was to evaluate the usefulness of sonoelastography (using 5-point scoring method and strain ratio) in improving the diagnostic performance of conventional ultrasound in indeterminate cases of US BI-RADS 3 & 4 breast lesions; to guide the diagnostic workup towards biopsy or follow-up.

90 female patients with breast lump on clinical examination and initially categorized as US BI-RADS 3 & 4 were included in this study with the mean patient age was 38.56 ± 14.06 years.

54 patients (60%) had benign lesions (pathologically proven); with the majority (45 of them) were fibroadenomas (83.3%). 36 patients (40%) had malignant lesions; with the majority (30 of them) were invasive ductal carcinoma (83.4%).

In our study we found that ES and SR were significantly higher in malignant breast lesions compared to benign lesions (p -value < 0.0001).

We found that; at a cutoff point = 4 for ES; the sensitivity was (91.7%); specificity (88.9%), positive predictive value (84.6%), negative predictive value (94.1 %) and total accuracy of about (90%). At a cutoff point=3.6 for SR; the sensitivity was (91.7%), specificity (77.8%), positive predictive value (73.3%), negative predictive value (93.3%) and total accuracy of about (83.3%); area under curve (AUC)=0.900, p -value= < 0.0001 .

Our results agreed with Kumm et al., 2010 [11] who examined 310 lesions in 288 female patients; the ES had sensitivity of about 76% and specificity 81%; and with a threshold of 4.5 for SR the sensitivity was 79% and specificity 76%. Accordingly; the study concluded that the sensitivity of SR was higher while specificity was higher in the scoring system; which is compatible with our study results.

In our study; three benign lesions (fibroadenomas) gave high ES (4) and SR (8-10) resulting in false positive results. The high strain ratio in these patients was probably due to the presence of coarse calcifications (confirmed on mammogram) thus making the lesion stiffer than it actually is. This agrees with Ioana A.G et al., 2011 [12] who found that fibroadenomas with calcifications have higher strain ratios comparable to malignant lesions.

We found three lesions with ES of 3 and SR of 3 which was found to be malignant on histopathology. The low strain ratio noticed in two patients with mucinous carcinoma could be attributed to intrinsic soft nature of the tumor. The third patient with false negative results and pathologically proven IDC; the lesion was deep (> 5 cms) which could interfere with accurate assessment of tissue stiffness by sonoelastography.

This agreed with a prospective study carried out in Romania; Ioana A.G et al., 2011 [12] who reported that one breast lesion (3.57%) with ES of 4 and one lesion (3.57%) with ES of 5 proved to be benign after histopathology. Additionally; one lesion (3.33%) with ES of 1 and three lesions (10.72%) with ES of 3 proved to be malignant after histopathology.

Our study results also agreed with that of Okar Atabey et al., 2014 [4] who examined 96 patients with 110 breast lesions by sonoelastography and used the 5 point scoring system; the specificity was found to be 83%, sensitivity 89%, positive predictive value 79% and negative predictive value 91%. Almost similar study results were stated by Parajuly et al., 2010 [13] who examined 342 lesions in 325 female patients using the 5 point scoring system with a threshold score between 3 and 4; they reported sensitivity of 77.7% and specificity 96.2% and with a threshold of 3.54 for SR; the sensitivity was 94.5% and specificity 94.3%.

The study of Sohn et al., 2009 [14] reported the sensitivity of conventional ultrasound as 98.2% and specificity as 44.1%; while if conventional ultrasound and ultrasound elastography were added together; the specificity increased to 50.5%. It was concluded that ultrasound elastography scoring system could increase the specificity of conventional breast ultrasound.

Our study results are compatible with that of Farooq F et al., 2019 [15] which stated that BIRADS assessment is enhanced by ultrasound elastography in distinguishing benign from malignant breast lesions.

Nearly similar results were reported by Mehmet Siddi et al., 2020 [16] who found that addition of sonoelastography to conventional B mode US could help to prevent unnecessary biopsies.

Reghunath et al., 2021 [17] also concluded that strain elastography could enhance the characterization of indeterminate US BI-RADS 3 & 4 lesions.

Conclusion:

Breast strain elastography using 5-point scoring method and strain ratio was found to be of high sensitivity, specificity and diagnostic accuracy in differentiating benign from malignant breast lesions initially categorized as US BI-RADS 3 & 4. It provides additional information on tissue stiffness to increase the diagnostic performance of conventional ultrasound in the setting of indeterminate BI-RADS 3 and 4 lesions. It is our recommendation to add elastography as a part of routine breast ultrasound exam using both elasticity score and strain ratio to increase the confidence of diagnosis and guide the diagnostic workup towards biopsy or follow-up and thus reducing the rate of unnecessary biopsies.

References

- 1- KOKUBU Y., YAMADA K., TANABE M., et al.: Evaluating the usefulness of breast strain elastography for intraductal lesions. *J. Med. Ultrasonics*, 48: 63-70. <https://doi.org/10.1007/s10396-020-01070-2>, 2021.
- 2- MUTALA T.M., MWANGO G.N., AYWAK A. et al.: Determining the elastography strain ratio cut off value for differentiating benign from malignant breast lesions: systematic review and meta-analysis. *Cancer Imaging* 22, 12. <https://doi.org/10.1186/s40644-022-00447-5>, 2022.
- 3- BOJANIC K., KATAVIC N., SMOLIC M., et al.: Implementation of elastography score and strain ratio in combination with B-mode ultrasound avoids unnecessary biopsies of breast lesions. *Ultrasound Med. Biol.*, 43: 804-16, 2017.
- 4- OKAR ATABEY A., AR•BAL E., ERGELEN R., et al.: Ultrason Elastografinin Meme Lezyonlarının Ayırıcı Tanısındaki Yeri ve Histopatolojik Korelasyon. *J. Breast Health*, 10: 234-238, 2014.
- 5- MATSUOKA Y., KAWAUCHI N., SUGINO N., et al.: The optimal cutoff value of elasticity index and ratio for discrimination between benign breast mass and invasive carcinoma on breast ultrasound. *J. Med. Ultrasonics.*, 44: 529-34, 2017.
- 6- LEE S.H., CHUNG J., CHOI H.Y., et al.: Evaluation of screening US-detected breast masses by combined use of elastography and color Doppler US with B-mode US in women with dense breasts: A multicenter prospective study. *Radiol.*, 285: 660-9, 2017.
- 7- UENO E., UMENOTO T., MATSUMURA T., et al.: New quantitative method in breast elastography: Fat lesion ratio (FLR). Paper presented at: Radiological Society of North America 93rd Scientific Assembly and Annual Meeting; November 25-30, Chicago, IL. November 27, 2007.
- 8- AHMED A.T.: Diagnostic utility of strain and shear wave ultrasound elastography in differentiation of benign and malignant solid breast lesions. *Egypt J. Radiol. Nucl. Med.*, 51: 70. <https://doi.org/10.1186/s43055-020-00181-7>, 2020.
- 9- PARK H.J., KIM S.M., YUN B., et al.: Comparison of one- and two-region of interest strain elastography measurements in the differential diagnosis of breast masses. *Korean J. Radiol.*, 4: 431-41. <https://doi.org/10.3348/kjr.2019.0479>, 2020;21.
- 10- UENO E.I.A.: Diagnosis of breast cancer by elasticity imaging. *Eizo Joho Medical*, 36: 2-6, 2004.
- 11- KUMM T.R. and SZABUNIO M.M.: Elastography for the characterization of breast lesions: Initial clinical experience. *Cancer Control.*, 17: 156-161. (PMID: 20664512), 2010.
- 12- IOANA A.G., STOICA Z. and BONDARI S.: Differential diagnosis of breast lesions using ultrasound elastography. *Indian J. Radiological Imaging*, 21: 301-5, 2011.
- 13- PARAJULY S.S., LAN P.Y., YAN L., et al.: Breast elastography: A hospital based preliminary study in China. *Asian Pac. J. Cancer Prev.*, 11: 809-14, 2010.
- 14- SOHN Y.M., KIM M.J., KIM E.K., et al.: Sonographic elastography combined with conventional sonography: How much is it helpful for diagnostic performance? *J. Ultrasound Medicine*, 28: 413-420. (PMID: 19321669), 2009.

- 15- FAROOQ F. and MUBARAK S.: Value of Elastography in Differentiating Benign from Malignant Breast Lesions. Keeping Histopathology as Gold Standard (October 08, 2019). Cureus 11(10): e5861. doi:10.7759/cureus.5861, 2019.
- 16- MEHMET SiDDiK YiLDiZ M.D. and CEMIL GOYA M.D.: Contribution of Sonoelastography to Diagnosis in Distinguishing Benign and Malignant Breast Masses. J. Ultrasound Med., 39: 1395-1403, 2020.
- 17- REGHUNATH A., MITTAL M.K., CHINTAMANI C., et al.: Novel approach in the evaluation of ultrasound BI-RADS 3 & 4 breast masses with a combination method of elastography & Doppler. Indian J. Med. Res., doi: 10.4103/ijmr.IJMR_1398_19. (PMID: 34854427), 2021.

دور قياس المرونة بالموجات فوق الصوتية فى زيادة كفاءة الموجات فوق الصوتية العادية فى تقييم آفات الثدي من التصنيف الثالث والرابع

تعد الإصابة بكتل الثدي من الإصابات الشائعة ويعد كلا من التصوير الإشعاعى للثدى والموجات فوق الصوتية من اختبارات الفرز الأكثر شيوعاً لكتل الثدي، ومع ذلك فكلاهما يعانى من بعض القصور.

قياس المرونة بالموجات فوق الصوتية هى التقنية التى تستخدم انضغاطية الانسجة للكشف عن تباين الانسجة التى يتم فحصها من حيث الصلابة، وتعتبر الآفات السرطانية أكثر صلابة من تلك الغير سرطانية.

ولقد هدفت هذه الدراسة لتقييم دور قياس المرونة بالموجات فوق الصوتية فى زيادة كفاءة الموجات فوق الصوتية العادية فى تقييم آفات الثدي من التصنيف الثالث والرابع وتوفير معلومات اضافية عن مرونة الأنسجة وذلك لتوجيه الخطوات التشخيصية أما لأخذ عينة أو متابعة المريض، ودراستنا استباقية شملت ٩٠ مريضة تعانى من كتل الثدي.

وقد وجدنا ان قياس المرونة بالموجات فوق الصوتية له حساسية ونوعية عالية فى التفرقة بين كتل الثدي الحميدة والخبيثة.

ولقد أوصينا بإضافة قياس المرونة بالموجات فوق الصوتية كجزء من فحص الثدي الروتينى بالموجات فوق الصوتية لإضافة مزيد من الثقة للتشخيص.