Research Article

Ultrasound strain Elastography of Normal Breast Tissue in Correlation with Mammographic Breast Density

Dr.Huda Fawzi Salih, *M.B.Ch.B , DMRD* [1]
Dr.Noor Kadhum Neema, *F.I.B.M.S / radiology* [2]
Dr.Suha Hussain Hayyawi, *F.I.B.M. , C.A.B.S/G.O* [3]
Dr.Wasan Ismail Al-Saadi, *F.I.B.M.S / radiology* [2]
[1] Radiology department , Al-Immamain Al-Kadhimain Medical City
[2] Radiology unit , Surgery department , College of Medicine, Al-Nahrain University
[3] Gynaecology & Obstetric department , Al-Immamain Al-Kadhimain Medical City

Date Submitted: 11/10/2016
Date Accepted:10/11/2016

Address for Correspondence:
e-mail :drwasan_72@yahoo.com

Abstract

Background: Strain elastography is relatively new ultrasound technique that assess elasticity of the tissue .This technique utilize the relative strain of the tissue of interest to generate color coded image and to measure the strain ratio. It has been extensively investigated and introduced as a promising technique for characterization of breast masses.

Aim of study: To assess the relative strain of fat and glandular tissue as well as the strain ratio in relation to different mammographic breast density categories and with respect to the depth of tissue

Subjects and Methods: A total of 162 women with normal breast imaging were included and categorized according to the American College of Radiologists (ACR) mammographic breast density categories (A, B , C , D). Elastography examination was performed for a single normal breast and the relative strain of the fatty tissue and glandular tissue at most superficial location as well as at 1-2 cm in depth were recorded . In addition the fat:glandular strain ratio was estimated. The elastographic variables were assessed with each other and with respect to breast density & the tissue depth

Results: The subjects were subdivided according to ACR density system. It has been found that the mean relative strain of fat was higher in category A (0.30) in comparison with the other categories with statistically significant difference , however the relative strain of the glandular tissue was rather comparable between category A (0.25), category B (0.24) and category C (0.22) with statistically significant difference with category D(0.20) .The strain ratio was significantly different in category B (1.10) and category C (1.05) in comparison with category A (1.22).Comparing the relative strain in different depth revealed rather similar results where relative strain of fat in (1- 2 cm) below Ref show significant difference in category B(0.21) and category C(0.20) in comparison with category A (0.29) as category group D is extremely dense so no fat tissue below ROI could be measured. Similarly the relative strain of glandular tissue in 1-2 cm below ROI show significant difference between category A (0.23) and category B (0.22) with category C and D (0.19 for both).

Conclusion: The fat tissue elasticity is rather different in different breast density categories with higher elasticity of the fat in category A breast density (fatty breasts) as compared to other breast density categories .The glandular tissue strain is rather more comparable in the breasts in category B, C, and D and thus it may more convenient to use the glandular tissue as a reference tissue when assessing the relative elasticity of breast masses. Moreover , the depth of the measurement of the tissue elasticity has a significant influence on the quantitative assessment of the elastographic image

Key words: strain elastography, ACR breast density, relative strain, strain ratio.

INTRODUCTION

Elastography is an imaging modality for detection of abnormal changes in soft tissue with assessment of tissue stiffness usually in terms of strain (the tissue tendency to change size or shape in response to external compression) , a property that was beforehand judged just subjectively by physical examination.[1-3] The technique is considered as the most important of the new advancements in ultrasound technology.[4] Until now this advanced technique was used to examine diseases in organs like breast, thyroid, liver and prostate,[5] and to aid in making a differential diagnosis as it can yield details not only about the morphologic features but also about the lesion hardness.[6] Perhaps the most common application of elastography in the current practice is at the field of breast diseases. Several clinical studies showed that different conditions, such as ageing, inflammation or presence of malignancy are generally well-correlated with differences in stiffness between surrounding normal and pathological tissues.[7-9] Many researches focused on the quantitative assessment , i.e. the strain ratio (SR) of breast masses in order to establish elastographic criteria to differentiate benign from malignant lesions;[10,11] however, different cutoff values for the SR were proposed and to date there is no standard cutoff point to make the distinction . Although the elastography is much to be considered as operator dependant technique , we believe that other factors as the variability of the breast density and the breast composition may have some contribution to the differences in SR values suggested by several studies . To the best of our knowledge , no previous study has dealt with the assessment of normal breast elasticity with respect to different breast density and composition. In this limited sample study we aimed at assessment of the relative strain of breast fat and fibroglandular tissue and relate the findings with the mammographic breast density to find out if the overall density of the breast affects the relative strain of each specific tissue at different depths.

PATIENTS AND METHODS

This was an analytic cross sectional study conducted at the breast clinic at al –Immamian al-kadhemain medical city , for the period from November 2015 to August 2016. The subjects of the study were recruited from the mammography unit after performance of mammography for different indications (screening or diagnostic purposes) . The patients were initially assessed and examined by a senior gynaecologist to determine the parity , the intake of hormonal replacement therapy , the previous breast surgery or chest wall irradiation and the presence of palpable breast abnormality . Only those subjects with at least one normal breast as confirmed by clinical examination , mammography and subsequent breast conventional sonography were included in the study . Those subjects with previous breast surgery, breast or chest irradiation , intake of hormonal replacement therapy , or with bilateral breast abnormality were excluded .

Only 162 females fitted into the inclusion criteria . The subjects were categorized according to the mammographic breast density into 4 groups (A-D) according to the American college of radiologist breast density categories,[12] where **Category A:** The breasts are almost entirely fatty,

Category B: There are scattered areas of fibroglandulardensity, **Category C:**The breasts are heterogeneously dense, which may obscure small masses , and **Category D:**The breasts are extremely dense, which lowers the sensitivity of mammography.

Elastography examination was performed for a single normal breast of each female and the relative strain of the fatty tissue at the subcutaneous area and the most superficially located glandular tissue were recorded as well as at 1-2 cm in depth . In addition the fat:glandular tissue strain ratio was estimated. The elastographic variables were assessed against each other for different tissue types at different depths and with respect to the mammographic breast density category

Examination equipment and technique

Both the B-mode imaging and the elastographic examinations were performed using ultrasound systems (GE Voluson E6) with high frequency linear probe . The patient was placed in the supine position , the arm is raised under head , the patient was instructed to have quiet respiration during the elastographic procedure to avoid the counter strain caused by forcible movement of the chest wall . At conventional B-mode scanning , the different types of normal breast tissue were defined , then elastography was initiated .

For elastographic examination, the region of interest (ROI) was set so that it include the different types of normal breast tissue(subcutaneous fat , retromammary fat and glandular tissue) .

The elastographic examination was accomplished by applying very light initial touch with the transducer perpendicular to the skin surface . After obtaining adequate images according to color task bar at the upper left corner , relative strain of the fat (Ref1) and

the glandular tissue (Ref2) were recorded at superficial sites and at 1- 2 cm in depth , then the strain ratio was obtained . Three measurements were obtained for each reference tissue and SR and the average value was recorded . Strain value was expressed as percentage (%) by the machine, but for the sake of simplicity we omitted the (%) for all numerical values represented in the results.

Statistical Analysis : Frequencies of that data are calculated and arranged in tables and figures using Microsoft excel 2013 . The data is checked and entered into statistical package for social science (SPSS), we used the version 17 in the analysis of our data, The data that had been collected are presented in simple cell. To determine the association between different variable, unpaired t test was used the determined these association where P value < 0.05% is considered as statistical significant

RESULTS

The study included 162 women with age range of 36-78 years (mean =47.25 years)

Clinically, 82 subjects were referred to breast clinic for screening mammography , while the remaining 80 subjects were referred for mammography for different complaints as mastalgia, nipple discharge or sensation of a lump.

Mammographic density assessment defined 58(35.8%) subjects to be at category A , 44 (27.1 %) subjects to be at category B ,52(32.2%) subjects to be at category C and 8 subjects (4.9 %) to be at category D (figure1)

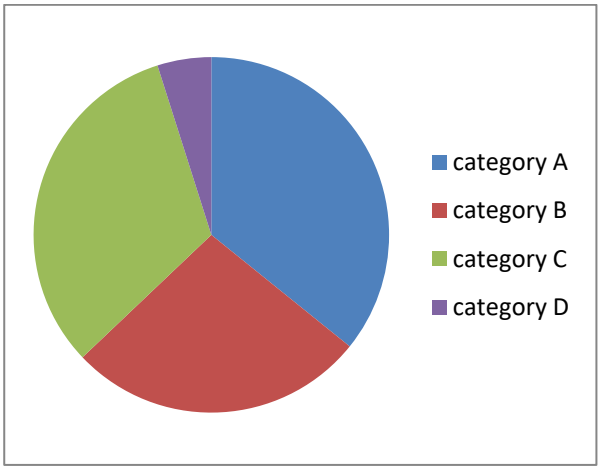

Figure 1: Patient distribution according to ACR breast density

The age distribution for the subjects in each group is illustrated in table (1)

Table (1): Age distribution of the study subjects in the 4 breast density category groups

Parameter	A N=58	B N=44	C N=52	D N=8
Age (yr) Mean±SD (Range)	52.14+10.74 (37-78)	49.73+8.16 (35-67)	44.23+5.38 (36-53)	42.25+6.73 (37-53)

The relative Strain value of fatty tissue and glandular tissue in the

four groups of study with strain ratio (Ref \ROI) :

The mean relative strain of fat was higher in group A in comparison with the other groups with statistically significant difference ,however the relative strain of the glandular tissue was rather comparable between group A, B and C with statistically significant difference with group D. On the other hand the strain ratio was significantly different in group B and C in comparison with group A (figures 2-4) .

Table 2: the relative strain of fatty and glandular tissue among 4 study groups by unpaired t-test

Parameter	A Mean±SD	B Mean±SD	C Mean±SD	D Mean±SD
Fat strain	0.30+0.11	0.25+0.08 *	0.23+0.11 *	0.22+0.04 *
Glandular tissue	0.25+0.11 **	0.24+0.11 **	0.22+0.09 **	0.20+0.03
Strain ratio	1.22 +0.36	1.10 +0.39*	1.05 +0.40*	1.13+0.17
1-2 cm below Ref (fat)	0.29+0.10	0.21+0.11 *	0.20+0.10 *	
1-2 cm below ROI (glandular)	0.23+0.10 **	0.22+0.12 **	0.19+0.08 *	0.19+0.06

***Significant difference with category A,**

****** mean significant difference with category D. (p <0.05)**

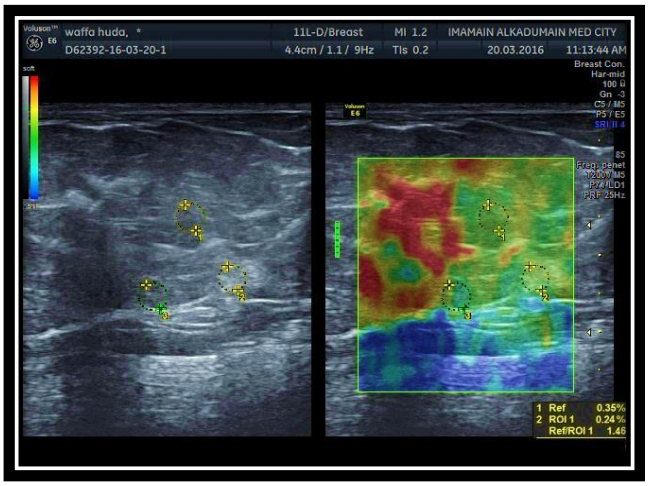

Figure 2: The relative strain ratio of fatty tissue & glandular tissue in fatty breast (category A) , yellow arrow point to fatty tissue , white arrow point to glandular tissue.

Figure 3: The relative strain ratio of fatty tissue & glandular tissue in category B breast , yellow arrow point to fatty tissue , white arrow point to glandular tissue.

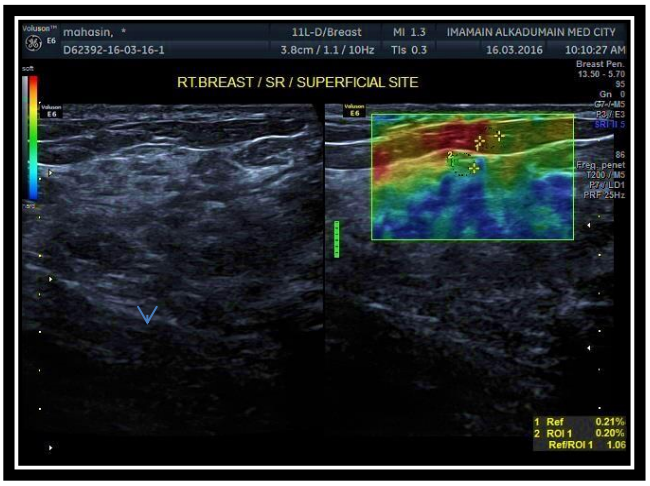

Figure 4: The relative strain ratio of fatty tissue & glandular tissue in dense breast (category C) yellow arrow point to fatty tissue , white arrow point to glandular tissue.

Comparing the same parameters at different depth revealed rather similar results where strain value of fat in (1- 2 cm) below Ref show significant difference in group B and C in comparison with A study group (as group D is extremely dense so no fat tissue below ROI could be measured) (table 3) (figure 5).Similarly the relative strain of glandular tissue in 1-2 cm below ROI show significant difference between group A and B with C and D (table 4) (figure 6)

Table 3: The relative strain of fatty tissue in superficial area (Ref) and deep area (1-2 cm below(P value < 0.05 is significant.)

	Superficial fat Mean±SD	**Deep fat Mean±SD**	**P value**
Category A	0.30+0.11	0.29+0.10	0.6339
Category B	0.25+0.08	0.21+0.11	**0.0409**
Category C	0.23 +0.11	0.20+0.10	**0.0496**
Category D	0.22+0.04	–	–

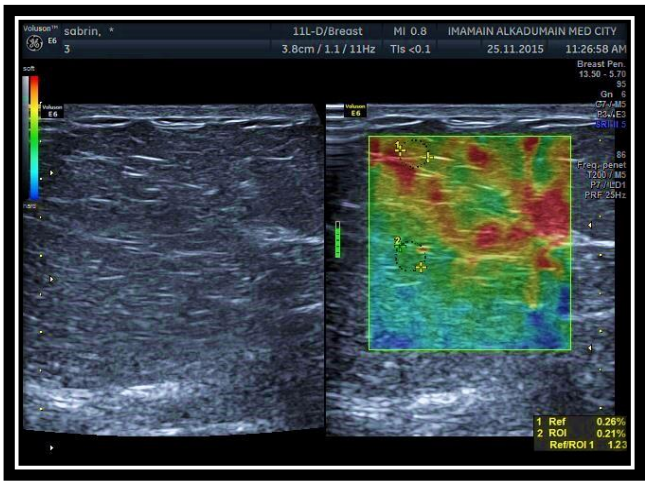

Figure 5: Measurement of relative strain of fatty tissue in superficial and deep areas in fatty breast (category A)

Table 4 :relative strain of glandular tissue in superficial area (Ref) and deep area (1-2 cm) below

Mammographic density	Superficial glandular Mean±SD	Deep glandular Mean±SD	P value
Category A	0.25+0.11	0.23+0.10	**0.0339**
Category B	0.24+0.11	0.22+0.12	**0.0461**
Category C	0.22 +0.09	0.19+0.08	**0.0496**
Category D	0.20+0.03	0.19+0.06	–

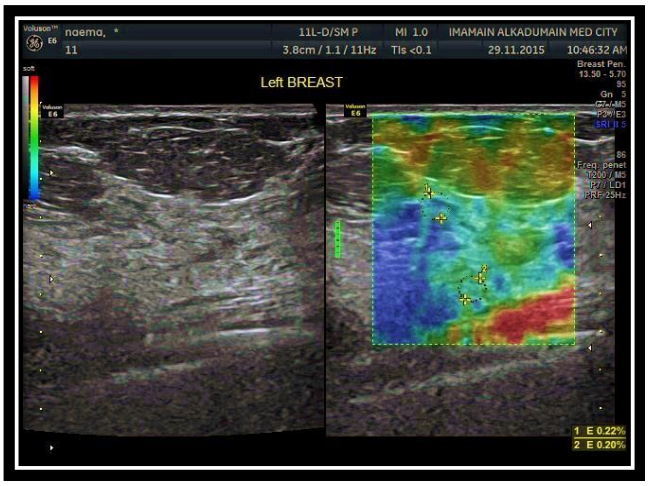

Figure 6: Measurement of relative strain of glandular tissue in superficial and deep areas .

DISCUSSION

Results Summary

The current study showed significant difference in the elasticity expressed as strain value and strain ratio of fatty and fibroglandular tissue with respect to different categories of breast density, in addition , significant difference in strain value of fatty tissue at different depths within the breast of the same density category was found . The elasticity of the fibroglandular tissue was found to be more comparable between different categories at different depths in comparison with that of the fatty tissue .

Results interpretation

In this study we have found that the relative strain of the breast fat at superficial position is different in each breast density category , where the strain is higher at category A and become less as we approach the higher density breasts with statistically significant difference. Upon assessing the glandular tissue relative strain on the other hand , it has been found that there is no significant difference in the glandular tissue relative strain between density groups B, C and D however the difference was statistically significant with group A that showed higher strain value of the glandular tissue indicating more elasticity .

Although we did not come across a similar study that compares the elasticity of different components of the breasts and correlates them with the mammographic breast density , we think that this issue is of utmost importance and it may contribute to the wide range of variations in the estimated cutoff values for differentiating benign from malignant lesions in the breast. Many of the researchers as Zhi et al,[10] yerli et al,[11] Kadhem and Tawfeq,[13] and Hawigi et al,[14] have found different mean SR for benign and malignant breast masses (1.8 , 2 , 2.4 , 1.29) for benign lesions and 8.3 , 5.9 , 5.6 , 4.06) for malignant lesions respectively) and suggested a different cutoff values of 3.05 , 3.5 , 3.2 and 2.5 respectively to be reasonably sensitive and specific to diagnose or exclude malignancy. This significant range of variability would definitely reduce the confidence level in the technique of elastography. Upon reviewing the methodology of these studies , it has been found that some of these researchers are using fat tissue as the reference tissue (Zhi et al,[10] Kadhem and Tawfeq[13] while others (yerli et al [11] and Hawigi et al,[14] are referring to the normal glandular tissue at their measurement. Looking back to the results of the current study one can easily judge that there are significant variations in the relative strain and SR at

different breast density categories particularly when comparing the extremely low density fatty breast with other categories .Subsequently it is expected that a mass arising within a dense breast would have different relative strain not only because of its cellular constituents , its size , its depth but also due to variability of the density of the harboring tissue .Unfortunately none of the previously mentioned studies had classified the patients according to ACR mammographic breast density.

Another factor investigated at this study was the effect of tissue location and depth on the relative strain and SR . We have found that the tissue strain is less at deeper location within the same density group and the difference that was encountered in strain values at superficial sites between different groups was also maintained at deep location .This finding indicates that the depth of measurement influences the results even if we are measuring the same type of tissue and this could be related to the accumulative effect of the increased tissue thickness as we make the measurement at deeper levels in addition to the impact of the presence of the overlying mammary fibroglandular tissue at deeper points in comparison with that at superficial location. The effect of the depth on the quality of the elastogram was investigated by several authors .Raza et al,[15] found that both false positive and negative results occurred when the breast lesions were located deeper than 12 mm. On the other hand Ciurea et al,[16] reported that the elastographic score was more accurate for superficial lesions than deep ones. The same conclusion was reached by Song et al,[17] who concluded that factors as depth of the lesion, the thickness of the tissue layer anterior to the lesion and the breast thickness at the location of the lesion were significantly associated with the quality of the elastogram. The aforementioned studies concluded that superficial lesions are more adequately and accurately assessed than deeply seated lesions and they all questioned the value of elastography in rather deeply located lesions.

In conclusion , the fat tissue elasticity is rather different in different breast density categories with higher elasticity of the fat in category A breast density (fatty breasts) as compared to other breast density categories .The glandular tissue strain is rather more comparable in the breasts in category B, C, and D and thus it may more convenient to use the glandular tissue as a reference tissue when assessing the relative elasticity of breast masses. Moreover , the depth of the measurement of the tissue elasticity has a significant influence on the quantitative assessment of the elastographic image

REFERENCES

1. Ophir J, Cespedes I, Ponnekanti H, Yasdi Y, Li X. Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrason Imaging 1991;13: 111-34.
2. Samani A, J. Zubovits, Plewes D. Elastic moduli of normal and pathological human breast tissues: an inversion-technique-based investigation of 169 samples. Phys Med Biol 2007; 52: 1565-76.
3. Frey H. Real time elastography. A new ultrasound procedure for the reconstruction of tissue elasticity.Der Radiologe 2003 ; 43: 850-5
4. Nakashima K., Shiina T, Sakurai M, EnokidoK,Endo T, Tsunoda H, et al. JSUM ultrasound elastography practice guidelines: breast. J Med Ultrason 2013 ;40(4): 359-391
5. Hussain MA, Alam F, Rupa SA et al. Lesion edge preserved direct average strain estimation for ultrasound elasticity imaging. Ultrasonics. 2014 Jan;54(1):137-46.
6. Tozaki M, Isobe S, Sakamoto M. Combination of elastography and tissue quantification using the acoustic radiation force impulse (ARFI) technology for differential diagnosis of breast masses. Jpn J Radiol 2012; 30(8):659-70.
7. Thomas A, Kümmel S, Fritzsche F et al. Real-Time Sonoelastography Performed in Addition to B-Mode Ultrasound and Mammography: Improved Differentiation of Breast Lesions? Acad Radiol 2006; 13: 1496- 1504.
8. Krouskop TA, Wheeler TM, Kallel F et al. Elastic moduli of breast and prostate tissues under compression. Ultrasound Imaging 1998; 20: 260- 274.
9. Varghese T. Quasi-Static Ultrasound Elastography. Ultrasound Clin. 2009; 4(3) : 323-338.
10. Zhi H., Ou B., Luo B. , Feng X., Wen Y. , Yang H.: Comparison of Ultrasound Elastography, Mammography, and Sonography in the Diagnosis of Solid Breast Lesions. J Ultrasound , Med 2007, 26, 807–815.
11. Yerli H, Yilmaz T, Kaskati T, Gulay H. Qualitative and semiquantitative evaluations of solid breast lesions by sonoelastography. J Ultrasound Med 2011 ; 30:179-86.
12. ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System, Reston VA, American College of Radiology; 2013.
13. Tawfeeq R.H , Nee·ma N.K, The Role of Strain Elastography in Differentiating Benign from Malignant Solid Breast Masses, A Thesis Submitted to the Iraqi Board for Medical Specializations in partial fulfillment of the requirement for the degree of fellowship in Radio-Diagnosis ,2015
14. Hawigi DH , Almosawi A. , Tawfeeq R. Role of ultrasound elastography in the assessment of breast masses. A dissertation submitted to the arab board for medical specialization as partial fulfillment of the requirement for fellow ship degree in radiology .2015
15. Raza S, Odulate A, Ong E, Chikarmane S, Harston CW. Using real time tissue elastography for breast lesion evaluation: our initial experience. *J Ultrasound Med* 2010; 29:551–563.)

16. Ciurea AI, Bolboaca SD, Ciortea CA, Botar-Jid C, Dudea SM. The influence of technical factors on sonoelastographic assessment of solid breast nodules.*Ultraschall Med* 2011; 32:27–34.

17. Guo Song, MD, Li Jing, PhD, Ma Yan, MD, Shang Cong, MD, Wang Xuejiao, MD. Influence of Various Breast Factors on the Quality of Strain Elastograms J Ultrasound Med 2015; 34:395–400