IMPACT OF ULTRASOUND ELASTOGRAPHY, IN THE DIAGNOSIS OF SOLID BREAST LESIONS.

Thesis
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By

Amany Abd Elhamid Abd Elhakam

Supervised by

Dr. Ahmed Mohamed Monib
Professor of Radiodiagnosis
Faculty of Medicine
Ain Shams University

Dr. Amr Mahmoud Abd ELsamad
Assistant professor of Radiodiagnosis
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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ABSTRACT

Breast cancer is a major health problem that warranted efforts to be paid in order to increase the diagnostic capability of the routinely used diagnostic aids. Ultrasound elastography is one of the newly introduced ultrasound built-in software that could increase the diagnostic capability of conventional ultrasound based on the fact that breast cancer is usually harder than benign breast lesions.

The routinely used method for classification of breast lesions according to tissue elasticity is the color coding as well as the strain ratio methods. Ultrasound elastography, does not only have a confirmatory diagnostic tool with sono-mammography, but also can be a beneficial technique by which ultrasound BIRADS downgrading of benign lesions could be elicited, thus reducing the number of unnecessary breast biopsies, and consequently improve the patients compliance .

However, ultrasound elastography has some limitations, such as operator dependency, inter, intraobserver variability, and results variability according to the internal structure of lesion being evaluated. So the cases should be evaluated as a whole regarding the history, clinical data, sono-mammographic findings, and ultrasound elastographic evaluation to attain the best diagnostic results, and to avoid false positive, and negative diagnoses.

Key words: Breast Lesions –Conventional Ultrasound – Ultrasound Elastography –Strain Ratio.

List of Abbreviations

ACR	***A**merican **C**olleague **of R**adiology*
ANDAI	***A**berration of **N**ormal **D**evelopment **A**nd **I**nvolution*
AUC	***A**rea **U**nder **C**urve*
BGR	***B**lue **G**reen **R**ed*
BIRADS	***B**reast **I**maging **R**eporting **A**nd **D**ata **S**ystem*
CC	***C**ranio- **C**audal*
C-plane	***C**oronal plane*
CAM	***C**ombined **A**uto-correlation **M**ethod*
CD	***C**olor **D**oppler*
CEUS	***C**ontrast **E**nhanced **U**ltrasound*
CI	***C**onfidence **I**nterval*
2-D	***T**wo - **D**imensional*
3-D	***T**hree - **D**imensional*
DCIS	***D**uctal **C**arcinoma **I**n **S**itu*
E	***E**lastoscore*
FM	***F**ibrocystic **M**astopathy*
FN	***F**alse **N**egative*
FNAC	***F**ine **N**eedle **A**spiration **C**ytology*
IDC	***I**nfiltrating **D**uctal **C**arcinoma*
LIQ	***L**ower **I**nner **Q**uadrant*
L/T ratio	***L**ongitudinal / **T**ransverse axis ratio*
LT.	***L**eft*
MLO	***M**edio **L**ateral **O**blique*
NPV	***N**egative **P**redictive **V**alue*
PPV	***P**ositive **P**redictive **V**alue*
RT.	***R**ight*
ROC	***R**eceiver **O**perating **C**haracteristic **C**urve*
ROI	***R**egion **O**f Interest*
SE	***S**onoelastography*
SR	***S**train **R**atio*
SSI	***S**upersonic **S**hear **I**maging*
TA	***T**otal **A**ccuracy*
TDLU	***T**erminal **D**uctal **L**obular **U**nit*
UE	***U**ltrasound **E**lastography*
UOQ	***U**pper **O**uter **Q**uadrant*
US	***U**ltrasound*

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Introduction and Aim of Work

Breast cancer is the most common female neoplasm (31% of tumors in females), and the second-leading cause of death among women. Breast lesions were first classified as malignant or benign categories ***(Catalano et al, 2009)***.

The most prevalent malignant lesions were further subdivided into three subgroups including: ductal carcinoma in situ (DCIS), invasive ductal carcinoma of nonscirrhous type, and invasive ductal carcinoma of scirrhous type ***(Itoh et al, 2006)***. Similarly, the most prevalent benign lesions were divided into three subgroups, including intraductal papilloma, fibroadenoma, and aberrations of normal development and involution (ANDI) ***(Itoh et al, 2006)***.

There have been marked advances in the quality of ultrasound imaging over the past 2 decades ***(Zhi et al, 2007)***. However the breast nodule is still a daily challenge for the radiologist in the setting of US diagnosis. This created the need for new diagnostic approaches including ultrasound elastography **(UE)** ***(Catalano et al, 2009)***.

The principle of elastography is that tissue compression produces strain (displacement) within the tissue, and that the strain is smaller in harder tissue than in softer tissue ***(Itoh et al, 2006)***. Therefore, by measuring the tissue strain induced by compression, ultrasound elastography (UE) can make the hardness of the tissue “visualize”, display its texture, and reflect the biological

characteristics of the mass. It shows promising prospects in differentiating benign from malignant breast tumor ***(Zhang et al, 2009).***

Today, real time elastographic systems that allow freehand scanning and provide excellent spatial resolution with less noise are integrated into commercially available US units. Benign tumors show even strain, whereas breast cancers show no strain in lesions or in surrounding areas ***(Cho et al, 2008).*** Elastography could also be used to distinguish an area of shadowing due to fibrosis from that due to carcinoma ***(Tan et al, 2008).***

The elastography strain images were scored according to the elasticity score in to five categories ***(Tan et al, 2008).*** Elasticity of breast tissue is affected by both physiological and pathological processes that cause structural changes as well as histological type of the mass being examined. Other factors that may affect the elasticity score are lesion size and depth. The more superficial the lesion, and the smaller its size, the more the sensitivity and specifity of yielded elastograms ***(Regini et al, 2010).***

Elastography allows for differentiation of malignant lesions from benign lesions (even among lesions smaller than 10 mm) ***(Itoh et al, 2006)***. Also it has the potential to evaluate the nature of the lesions detected at screening mammography and associated with microcalcifications, whether benign or malignant ***(Cho et al, 2009).***

Axillary lymphadenopathies are the single most important prognostic factor for operable breast cancer ***(Catalano et al, 2009).*** Elastography can provide useful information about the nature of lymph nodes and the quantitative

technique of the elastography further makes the diagnosis more accurate than B-mode, color and power Doppler sonography alone ***(Zhang et al, 2009).***

Frequently cystic alterations of the breast are interpreted as indeterminate nodules by the conventional approach, particularly those with a thick fluid content, fine debris in suspension, or complex cysts with mural nodules ***(Fleury et al, 2008).***

Combination between UE, conventional sonography, and mammography facilitate detection of two features of a lesion, morphologic characteristics and hardness, which reflect the properties of the lesion, facilitating differentiation between benign and malignant tumors, and thus elevating the sensitivity, specificity, accuracy, and the positive predictive value, augmenting the diagnostic capability of sonomammography ***(Zhi et al, 2007)***.

UE is better than sonomammography for detecting breast cancer in small sized breasts ***(Zhi et al, 2007).*** Also elastography has a higher sensitivity compared with B-mode US in the presence of breast lipomatous involution ***(Thomas et al, 2006).*** However, when using UE, one should pay attention to all the factors that would affect the stiffness of lesions such as large-scale necrosis, coarse calcifications, or organized hemorrhage, which may increase the hardness of the lesion, and cause misleading results ***(Zhi et al, 2007).***

Elastography was found to be superior to B-mode US in evaluating BI-RADS 3 **(Breast Imaging Reporting and Data System)** benign lesions ***(Thomas et al, 2006)***. Prevention of unnecessary histopathologic confirmation of breast lesions of BI-RADS 3 or 4 corresponding with elasticity scores 2, is one of the most important advantages. Additionally, a 6-month follow-up is

not necessary in case of BI-RADS 3 in conventional B-mode US and elasticity scores 2. Both situations provide a downgrading of the lesion to category BI-RADS 2. This may support the compliance of women, and also reduces costs in the health care system ***(Schaefer et al, 2011).***

There is very good inter-observer agreement in evaluating elastograms, which makes the method amenable to standardized interpretation ***(Thomas et al, 2006),*** however some authers documented that the inter-observer variability and image quality can influence performance. Future research will be critical to understand whether training and experience can ameliorate these effects ***(Burnside et al, 2007).***

Sonoelastography is not, however, free of limitations. These include high level of operator dependency, subjective interpretation of elastograms and sensitivity to slight changes in patient position ***(Regini et al, 2010).*** In summary, recent improvements in breast ultrasound equipment technology have occurred including the introduction of UE, which is very promising complementary diagnostic tool. Breast ultrasound is still being developed further, and this will lead to further better diagnostic approaches ***(Tohno et al, 2008).***

Aim of work

The aim of this study is to detect the impact of ultrasound elastography in diagnosis of solid breast lesions, and to evaluate its capability in differentiating benign form malignant lesions, with special focus on:

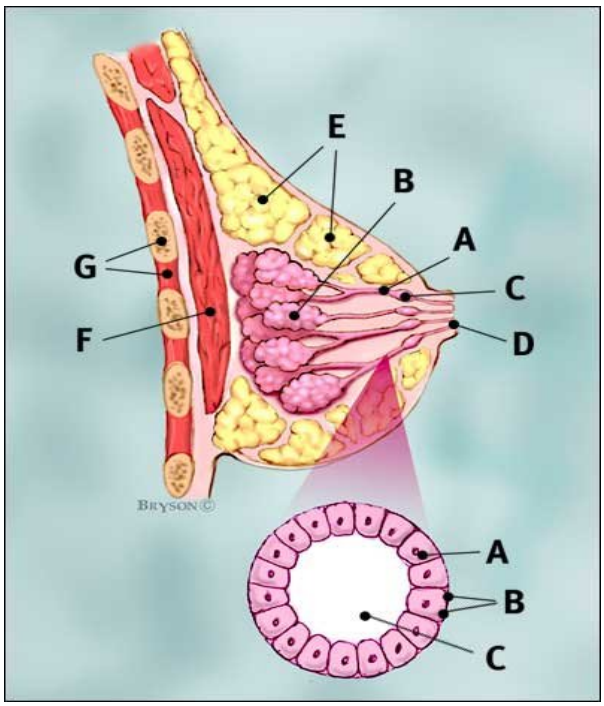
A-Evaluation of sensitivity and specificity of sonoelastography, with cyto-histological diagnosis taken as the reference.

B-Detection of the ability of sonoelastography to provide additional information on tissue elasticity in the event of equivocal mammographic and/or sonographic findings in order to guide the diagnostic workup towards biopsy or follow-up.

Anatomy of the Breast

The breast or mammary gland is a modified sweat gland that has the specific function of milk production ***(De Paredes, 2007).***

The adult breast is composed of three basic structures: the skin, the subcutaneous fat, and the breast tissue, which includes the parenchyma and the stroma. Beneath the breast is the pectoralis major muscle, the breast parenchyma is enveloped by deep and superficial fascial layers; Cooper's ligaments, the fibrous strands that support the breasts, traverse the parenchyma and attach to the fascial layers. The parenchyma is divided into 15 to 20 segments, with each drained by a lactiferous duct **(Fig. 1-1).** The lactiferous ducts converge beneath the nipple, with about 5 to 10 major ducts draining into the nipple. Each duct drains a lobe composed of 20 to 40 lobules ***(De Paredes, 2007).***



A- Ducts,
B- Lobules
C- Dilated section of duct to hold milk
D- Nipple
E- Fat
F- Pectoralis major muscle
G- Chest wall/rib cage.
(Supplied on line via: www.breastcancer.org/pictures/breast_anatomy/image_1.jsp)

Figure (1-1) Breast profile:

Wellings* & *Wolfe further classified the microstructure of the normal breast into the terminal duct lobular unit (**TDLU**) **(Fig. 1-2).** Small branches of the lactiferous ducts lead into terminal ducts that drain a single lobule. The terminal duct is composed of the extralobular segment and the intralobular segment. The lobule is composed of the intralobular terminal duct and the blindly ending ductules ***(Wellings* & *Wolfe 1978).*** The ductules are lined by a single layer of epithelial cells and a flattened peripheral layer of myoepithelial cells. A loose fibrous connective tissue stroma supports the ductules of the lobule ***(Wellings & Wolfe, 1978).***

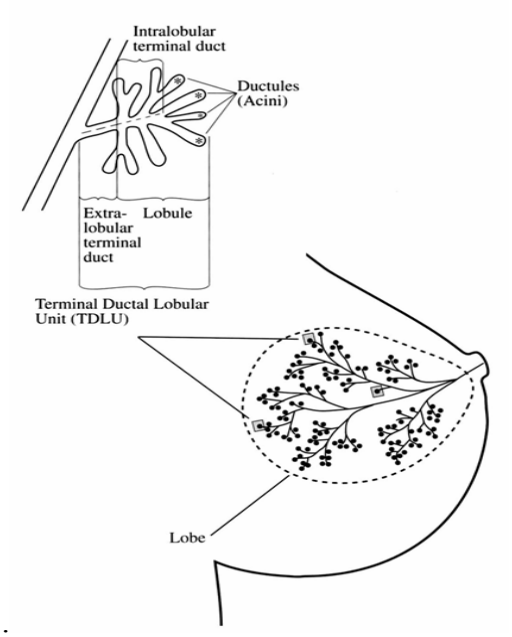


Figure (1-2): Anatomy of the human breast, a lobe and a TDLU.
(Supplied on line via: herkules.oulu.fi/isbn9514270525/html/c161.html)

Blood Supply and Lymphatic Drainage

The *primary arterial supply* to the breast is from the perforating branches of the internal mammary and lateral thoracic arteries. Minor contributions to the blood come from the branches of the thoracoacromial, subscapular, and thoracodorsal arteries. *Venous drainage* is primarily via branches of the internal mammary, intercostal, and axillary veins. The venous drainage of the breast is mainly to