Sudan University of Science and Technology
College of Graduate Studies

Study of Using Ultrasonography and Tomosynthesis Criteria of Breast Lesions: Radiologic-Histopathologic Correlation

دراسة إستخدام معايير الموجات فوق الصوتية والتصوير الطبقي ثلاثي الابعاد لأورام الثدي "والارتباط الاشعاعي – النسيجي المرضي

A thesis submitted for fulfillment of the requirements of PhD degree in Diagnostic Medical Ultrasound

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الآية

بسم الله الرحمن الرحيم

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Dedication

I dedicate this work to the soul of my father

To my lovely mother

To my wonderful husband for his patience, encouragement and continues support

To my children Zain, Lina and Ahmad for dreaming proudly About their father holding a PhD degree

To my brothers and sisters

To my best friends for them

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Abstract

This study aimed to utilize ultrasonography and digital breast tomosynthesis features of breast lesions for characterization and differentiation between benign and malignant and correlate these criteria with histopathological findings.This is prospective hospital base study performed in the breast imaging facility at radiology department, at King Abdul-Aziz Specialist Hospital (KAASH), Taif city, Saudi Arabia during the period from March 2015 to September 2017 included 200 female patients with 227 breast lesions who underwent digital mammography (Selenia Dimensions System; Hologic, Bedford, MA, USA) , ultrasound and ultrasound guided biopsy using a LOGIQ 7 unit (GE Healthcare) with a 12-MHz linear transducer, Core needle biopsy was performed by radiologists under ultrasound guidance using14-gauge Monopty device (Bard, Tempe, AZ) with a 10-cm needle Suros 9-gauge vacuum-assisted CNB biopsy device (Hologic). Data analysed using SPSS version 20. The results of this study revealed that the mean age of the patients was 43 years ranged from 25-82 years. 227 indeterminate (Bi-RADS category 3) or suspicious breast lesions (Bi-RADS category 4 and 5) were found. Of these lesions, 71 were confirmed as malignant and 152 had benign histopathological features.US description of the lesions including mass shape, echo pattern,

margin, boundary, orientation, posterior acoustic features, and calcifications as well as their power Doppler flow criteria are demonstrated. DBT descriptor breast density, nipple retraction, presence of calcification and its shape, architectural distortion and lesion criteria regarding the probability of malignancy, it was determined according to Bi-RADS for all lesions. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the grey scale US, DBT descriptors and power doppler criteria. Taking Bi-RADS category 4 as a cut point, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the lesions estimated Bi-RADS category as an indicator of malignancy. Then, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the lesions combining their Bi-RADS category and presence of penetrating vessels as indicators of malignancy. It concluded that Breast US is a useful diagnostic tool in breast cancer detection and can be used to characterize breast lesions. The vascular flow patterns of breast lesions on PDUS provide additional benefit for the differentiation of benign and malignant breast lesions.

مستخلص الدراسه

هدفت هذه الدراسة إلى استخدام الموجات فوق الصوتية واشعة الثدي ثلاثية الابعاد الرقميه في اورام الثدي للتوصيف والتمييز بين الحميدة والخبيثة وتربط هذه المعايير بالنتائج المرضية النسيجية. هذه دراسة اجريت في مرفق تصوير الثدي في قسم الأشعة ، في.مستشفى الملك عبد العزيز التخصصي ((KAASH، مدينة الطائف ، المملكة العربية السعودية خلال الفترة من مارس 2015 إلى سبتمبر 2018 ، ضمت 200 مريضة مصابة باورام الثدي 227 اللاتي خضعن لتصوير الثدي الرقمي (نظام أبعاد السيلينيوم ، هولوجيك ، بدفورد ، MA ، الولايات المتحدة الأمريكية) ، الموجات فوق الصوتية والموجات فوق الصوتية خزعة موجهة باستخدام وحدة (GE Healthcare) LOGIQ 7 مع محول خطي بقوة 12 ميجاهرتز ، تم إجراء خزعة إبرة أساسية بواسطة أخصائي الأشعة بإستخدام الموجات فوق الصوتية و جهاز ®Monoptyقياس 14-قياس (Bard، Tempe، (AZمع إبرة 10 Suros 9 جهاز قياس الخزعة CNB بمساعدة الفراغ .تحليل البيانات تم باستخدام SPSS الإصدار 20. أظهرت نتائج هذه الدراسة أن متوسط عمر المرضى كان 43 سنة تراوحت بين 25-82 سنة. تم العثور على 227 غير محدد (الفئة 3 من البايراد أو اورام الثدي المشبوهة (الفئة 4 و 5). من هذه الاورام، تم التأكد من وجود 71 حالة خبيثة و 152 منها تتميز بميزات نسيجية حميدة.وتم عرض وصف لهذه الاورام بما في ذلك شكل الكتلة ، ونمط الصدى ، والهامش ، والحدود ، والتوجه ، والسمات الصوتية الخلفية ، والتكلسات ، وكذلك معايير تدفق دوبلر الخاصة بالطاقة . الكثافة الثديية DBT ، سحب الحلمة ، وجود التكلس وشكله ، التشوه المعماري ومعايير الورم فيما يتعلق باحتمال الورم الخبيث ، تم تحديده وفقًا لـ Bi-RADS لجميع الآورام . تم حساب الحساسية ، والنوعية ، والقيمة التنبؤية الإيجابية والقيمة التنبؤية السلبية من أجل المقياس المعتمد لدى الولايات المتحدة ، مواصفات DBT ومعاييرقدرة الدوبلر مع أخذ الفئة 4 Bi-RADS كنقطة قطع ، تم حساب الحساسية والنوعية والقيمة التنبؤية الإيجابية والقيمة التنبؤية السلبية المقدرة فئة Bi-RADS

كمؤشر على الورم الخبيث. بعد ذلك ، تم حساب الحساسية والنوعية والقيمة التنبؤية الإيجابية والقيمة التنبؤية السلبية التي تجمع بين فئة Bi-RADS ووجود الأوعية المخترقة كمؤشرات للأورام الخبيثة. وخلصت إلى أن الموجات فوق صوتية واشعة تصوير الماموقرام ثلاثي الابعاد الرقمي أداة تشخيصية مفيدة في الكشف عن سرطان الثدي ويمكن استخدامها لتوصيف اورام الثدي. توفر أنماط تدفق الأوعية الدموية من آفات الثدي على فائدة إضافية لتمييز آفات الثدي الحميدة والخبيثة.

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2D	2-dimensional
3D	3-dimensional
ACR	American college of radiology
BIRADS	Breast Imaging Reporting and Data System
CC	Cranio caudal
DBT	Digital Breast tomosynthesis
DCIS	Ductal carcinoma in situ
DM	Digital mammography
DSCV	Digital spot compression views
FBCs	Fibrocystic changes
FNA	fine needle aspiration
FDA	Food and Drug Administration
FFDM	full-field digital mammography
IDC	Invasive ductal carcinoma
KAASH	King Abdul-Aziz Specialist Hospital
KV	Kilo voltage
MG	Mammography
MA	Mille amber
MLO	Medio lateral oblique
MRI	Magnetic resonance imaging
NCI	National cancer institute
PDUS	Power Doppler ultrasound
PPV	Positive predictive value
U/S	Ultrasound
USA	United states of America
PRLR	prolactin receptor
SNCR	Saudi National Cancer Registry
WCR	World Cancer Report

CHAPTER ONE

Chapter one

1. Introduction:

There are several types of tumours that may develop within different areas of the breast forming breast masses which are common in female. Most tumours are the result of benign (non-cancerous) changes within the breast while amongst all the breast masses, malignant masses are the most feared (Mieszkowski2004)

Breast cancer is the most common cause of cancer in women and the second most common cause of cancer death in women in the USA (United States of America). Breast cancer refers to cancers originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk(Ganesh N.etal 2010).

Worldwide, breast cancer comprises (10.4%) of all cancer incidences among women, making it the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer death. In 2004, breast cancer caused (519,000) deaths worldwide (7%) of cancer deaths; almost 1% of all deaths). Breast cancer is about 100 times more common in women than in men, although males tend to have poorer outcomes due to delays in diagnosis (Ganesh N.et al. 2010).

Saudi Arabia is no exception, where cancer of breast is most commonly prevalent. In one of the epidemiological studies conducted by(Ravichandran et al2005), who reported that the incidence of breast cancer in Saudi Arabia was (19.8%) of all the female cancers detected in the Kingdom(Al-Qahtani.2007).

According to a report of Saudi National Cancer Registry (2000-2004), the incidence of breast cancer was 127.8per 100,000 women and the mortality rate was reported as 25.5 per 100,000 (SEER Cancer Statistics

Review2018)5. A total of 7251 histologically confirmed new cases of cancer (4117 males and 3134 females) were seen in the 6-year period (1979 to 1984) in Riyadh (Al-Idrissi1991).

In 1951 Wild and Reid(Wild J et al1952)7, first developed equipment specially designed for breast scanning limited for differentiating between solid and cystic lesions, now, breast ultrasound proposes an attempt to characterize the breast ultrasound. The use of ultrasound in addition to clinical examination and mammography may result in an increased rate of breast cancer detection (Seidman H et al1987).

Breast ultrasound is of particular importance in those patients under 30 years of age as it is the usual initial breast imaging modality for them in many countries (Rania M et al 2018).

Mammography (MG) is the only effective screening method proven to lower mortality in up to 30%; it is an accessible, low-cost, low-radiation method (Liberman L et al1998).

Nonetheless, cancer is not visualized in 10% to 30% of cases. MG is incredibly useful, but not enough for accurate detection. Ultrasound, along with mammography, can increase breast cancer detection rates particularly among high-risk women and in those with denser breasts (60,70).The sensitivity of full-field digital mammography (FFDM) for the detection of breast cancer varies from (75% to 90%), while the specificity varies from 90% to 95% (Vaughan CL.2011) .

One of the shortcomings of traditional X-ray mammography is that it performs poorly when the breasts are dense – often the case for younger women who are less than 50 years of age – and the sensitivity falls to less than 50% (Kelly KM…et al ,2013).

Breast tomosynthesis is a new technology of digital mammography that enables the acquisition of a three-dimensional volume of thin section data, and thus reduces or eliminates tissue overlap,such ability allows visualization of cancers not apparent by conventional mammography and differentiation between benign and malignant lesions (Dobbins…et al 2009).

1.2 Problem of the study:

Masses especially palpable one in a woman's breast represents potentially a serious lesion and requires prompt evaluation.

The difficulty to differentiate the different types of breast lesions by conventional mammography and the researcher advised to add new tomosynthesis system and ultrasound.

1.3. Objectives

1.4. General objective:

The purpose of this study was to evalute the role of Digital Breast tomosynthesis (DBT) and ultrasound to utilize their features of breast lesions for characterization and differentiation between benign and malignant ones and correlating these criteria with histopathological findings.

1.4.1. Specific objectives:

- To find out the Digital Breast tomosynthesis imaging findings of benign and malignant breast lesions to better recognize these lesions
- To study the US imaging findings of benign and malignant breast lesions to better recognize these lesions:
- To concentrate the power Doppler flow criteria of breast lesions.
- To evaluate the accuracy of ultrasonography and Digital Breast tomosynthesis BI-RADS in the characterization of breast lesions.

1.4 Research outline:

The research included five chapters. Chapter one deal with the general introduction about the research, problem statement and the objectives of the study. Chapter two deals with literatures review cover the theoretical background and previous studies. Chapter three deal with the methodology of the study, including materials, method and equipment. Chapter four will cover the results. And chapter five covers discussion, conclusion, recommendation, references and appendices.

Chapter Two

CHAPTER TWO

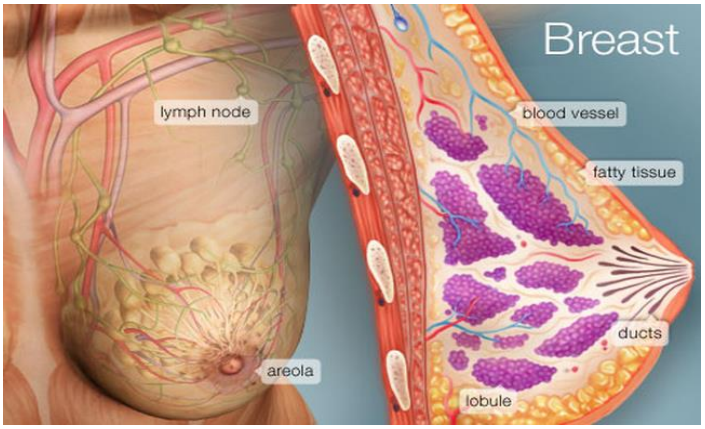
Literature review back ground

Anatomy,-Physiology,-Pathology

2.1.1Anatomy:

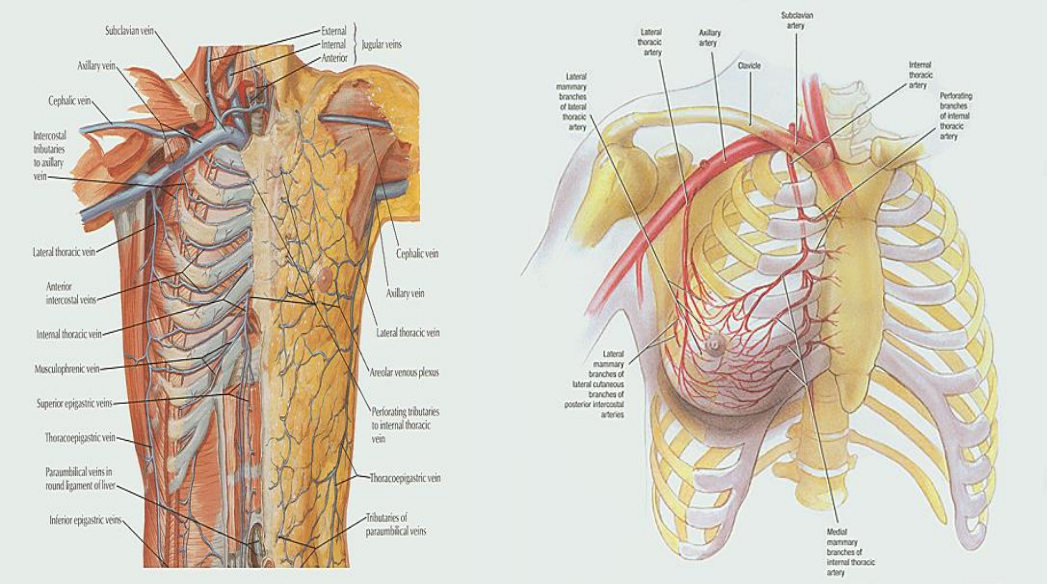
The breast is composed of two main types of tissues i.e., glandular tissues and stromal (supporting) tissues. Glandular tissues house the milk-producing glands (lobules) and the ducts (the milk passages) while stromal tissues include fatty and fibrous connective tissues of the breast. The breast is also made up of lymphatic tissue-immune system tissue that removes cellular fluids and waste. (Ganesh N et al .2010)

The breast is the tissue overlying the chest (pectoral) muscles. Women's breasts are made of specialized tissue that produces milk (glandular tissue) as well as fatty tissue. The amount of fat determines the size of the breast. The milk-producing part of the breast is organized into 15 to 20 sections, called lobes. Within each lobe are smaller structures, called lobules, where milk is produced. The milk travels through a network of tiny tubes called ducts. The ducts connect and come together into larger ducts, which eventually exit the skin in the nipple. The dark area of skin surrounding the nipple is called the areola (figure2.1).(Niklason LT, et al1997).



Fig(2.1): Breast anatomy .(Niklason LT, et al1997).

Arteries carry oxygen rich blood from the heart to the chest wall and the breasts and veins take de-oxygenated blood back to the heart. The axillary artery extends from the armpit and supplies the outer half of the breast with blood; the internal mammary artery extends down from neck and supplies the inner portion of the breast(figure2A,2B)(Netter F.H 2006) .



Fig(2.2) : Lateral & Internal Thoracic Vv and Aa.(Netter F.H 2006).

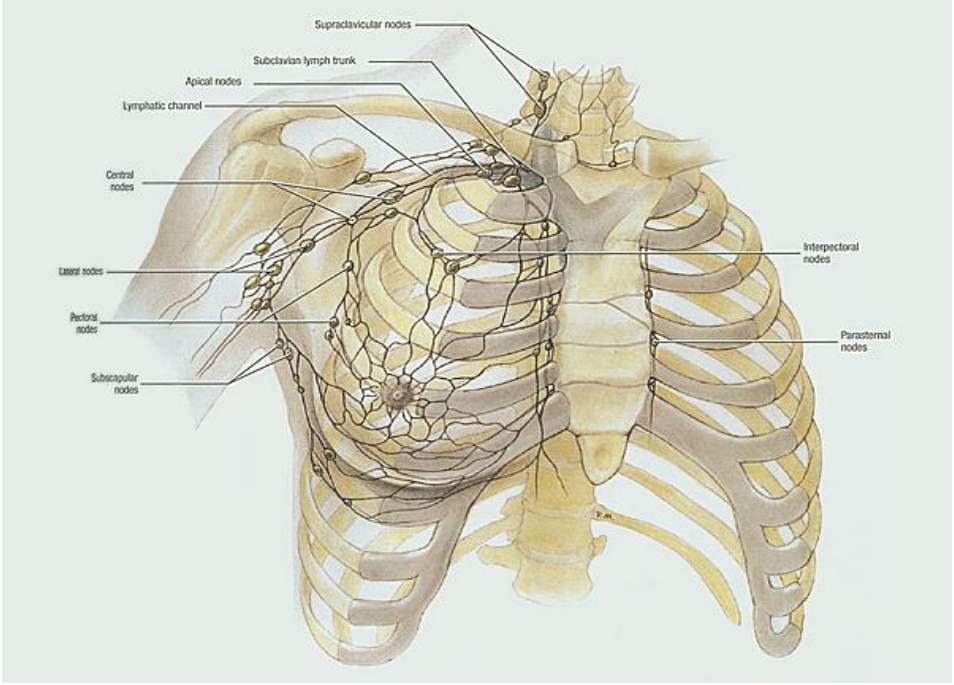
2.1The Lymph System:

Within the adipose tissue is a network of ligaments, fibrous connective tissue, nerves, lymph vessels, lymph nodes, and blood vessels. The lymph system, which is part of the immune system, is a network of lymph vessels and lymph nodes running throughout the entire body(figure2.2). Similar to how the blood circulatory system distributes elements throughout the body, the lymph system transports disease-fighting cells and fluids. Clusters of bean-shaped lymph nodes are fixed in areas throughout the lymph system and act as filters by carrying abnormal cells away from healthy tissue. (Clemente, C 2006)

Lymph Nodes of the Breast

Pectoral (anterior) nodes, Subscapular (posterior) nodes, Humeral (lateral) nodes, Central nodes, Apical nodes, Interpectoral (Rotter's) nodes

And Parasternal nodes



Fig(2.3): Clinical Anatomy of the Breast.(Netter F.H 2006).

2.1.2Nerves of the Breast

Cutaneous innervation, Medial pectoral nerve, Lateral pectoral nerve and Long thoracic nerve. (Netter F.H 2006).

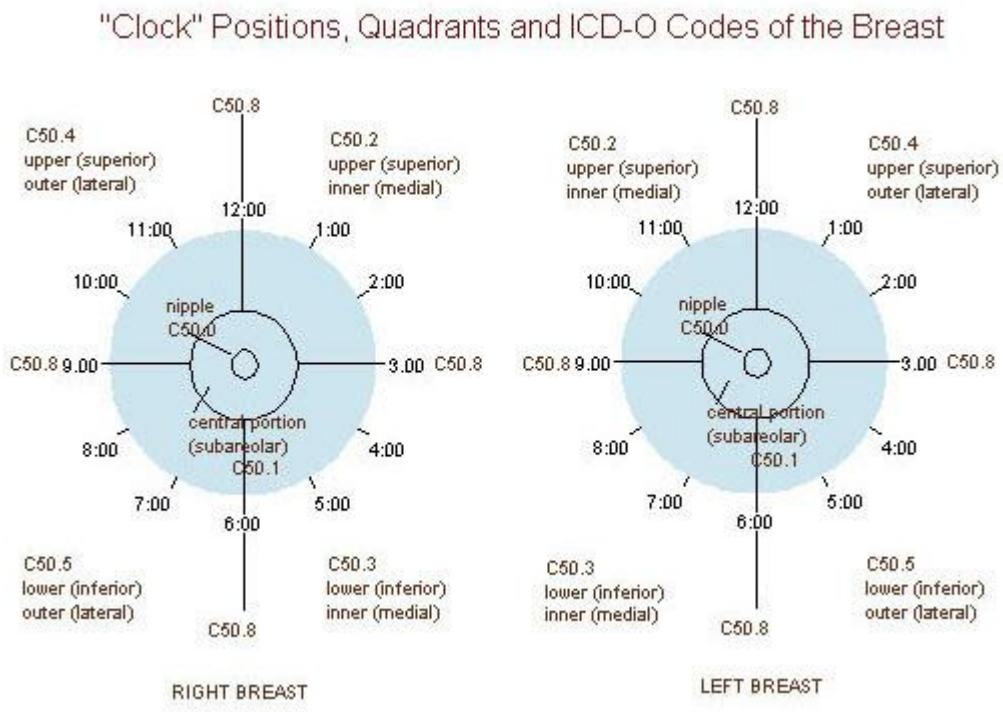


Fig (2.4): Clock positions, Quadrants and ICD-O codes of the breast**.** (Park JM 2007).

2.2Physiology:

Breast development, also known as mammogenesis, is a complex biological process in primates that takes place throughout a female's life. It occurs across several phases, including prenatal development, puberty, and pregnancy.

At menopause, breast development ceases and the breasts atrophy. Breast development results in prominent and developed structures on the chest known as breasts in primates, which serve as both a sexual characteristic and as mammary glands. The process is mediated by an assortment of hormones (and growth factors), the most important of which include estrogen, progesterone, prolactin, and growth hormone (Helvie MA 2010).

The function of producing milk is regulated by hormones. Stimulation of the female sex hormone, estrogen, causes the development of glandular

tissue in the female breast during puberty. Increase estrogen levels during pregnancy causes the breast size to increase in size through the accumulation of adipose tissues, Presence of progesterone stimulates the growth and maturation of the duct system. During pregnancy levels of estrogen and progesterone rises (levels are needed to sustain pregnancy) that further enhances the development of the mammary glands. This is the main reason why pregnant women has larger and more enhanced breast (Hynes NE et al 2010).

Development of the breasts during the prenatal stage of life is independent of biological sex and sex hormones (Leonard R2003).

During embryonic development, the breast buds, in which networks of tubules are formed, are generated from the ectoderm (Anthony W2014). These rudimentary tubules will eventually become the matured lactiferous (milk) ducts, which connect the lobules (milk "containers") of the breast, grape-like clusters of alveoli, to the nipples (Susan2014).

Until puberty, the tubule networks of the breast buds remain rudimentary and quiescent (Helvie MA 2010).

and the male and female breast do not show any differences (Leonard R2003)

During pregnancy, pronounced breast growth and maturation occurs in preparation of lactation and breastfeeding. (Helvie MA 2010).

Estrogen and progesterone levels increase dramatically (Leonard R2003), reaching levels by late pregnancy that are several hundred-fold higher than usual menstrual cycle levels(Horst-D2013). Estrogen and progesterone cause the secretion of high levels of prolactin from the anterior pituitary (Tefan S 2011),which reach levels as high as 20 times greater than normal menstrual cycle levels(Horst-D2013).

During lactation, Upon parturition (childbirth), estrogen and progesterone rapidly drop to very low levels, with progesterone levels being undetectable, while prolactin levels remain elevated. As estrogen and progesterone block prolactin-induced lactogenesis, by suppressing prolactin receptor (PRLR) expression in breast tissue, specifically, their sudden absence results in the commencement of milk production and lactation by prolactin(Leonard R2003).

2.3Pathology:

Breast diseases can be classified either with disorders of the integument, or disorders of the reproductive system. A majority of breast diseases are noncancerous (Barbara Fadem 2007).

A breast neoplasm is an abnormal mass of tissue in the breast as a result of neoplasia. A breast neoplasm may be benign, as in fibroadenoma, or it may be malignant, in which case it is termed breast cancer. Either case commonly presents as a breast lump. Approximately 7% of breast lumps are fibroadenomas and 10% are breast cancer, the rest being other benign conditions or no disease (Mitchell et al 2016).

2.3.1Benign Breast Diseases

2.3.1.1Mammary duct ectasia:

also called periductal mastiti A distinctive clinical entity that can mimic invasive carcinoma clinically. It is a disease of primarily middle-age to elderly parous women35 -36 Mammary duct ectasia is usually an asymptomatic lesion and is detected mammographically because of microcalcifications (Sweeney DJ, et al1995).

2.3.1.2Fat Necrosis:

Fat necrosis of the breast is a benign nonsuppurative inflammatory process of adipose tissue. It can occur secondary to accidental or surgical trauma, or it may be associated with carcinoma or any lesion that provokes

suppurative or necrotic degeneration, such as mammary duct ectasia and, to a lesser extent, fibrocystic disease with large cyst formation (Rosai J 2014**;** -Kinoshita T,et al 2002).

2.3.1.3Fibrocystic changes (FCCs):

Constitute the most frequent benign disorder of the breast. Such changes generally affect premenopausal women between 20 and 50 years of age (Diesing D2004)32, FCCs comprise both cysts (macro and micro) and solid lesions, including adenosis, epithelial hyperplasia with or without atypia, apocrine metaplasia, radial scar, and papilloma(Dupont WD, et al 1985).

2.3.1.4Cysts

Cysts are fluid-filled, round or ovoid structures(figure5) that are found in as many as one third of women between 35 and 50 years old. Although most are subclinical "microcysts," in about 20%–25% of cases, palpable (gross) cystic change, which generally presents as a simple cyst, is encountered cysts cannot reliably be distinguished from solid (O'Malley FP, et al,2004).

Masses by clinical breast examination or mammography; in these cases, ultrasonography and fine needle aspiration (FNA) cytology, which are highly accurate, are used. Cysts are derived from the terminal duct lobular unit. In most cysts, the epithelial lining is either flattened or totally absent. In only a small number of cysts, an apocrine epithelial lining is observed. Because gross cysts are not associated with an increased risk of carcinoma development (O'Malley FP, et al,2004).

Complex (or complicated or atypical) cyst is a sonographic diagnosis that is characterized by internal echoes or thin septation, thickened and/or irregular wall, and absent posterior enhancement (Houssami N, et al,2005).

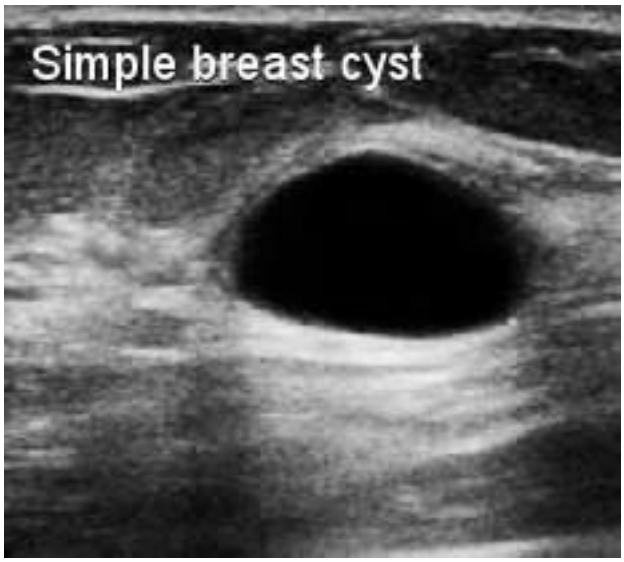


Fig (2.5): simple breast cyst (Houssami N, et al,2005).

2.3.1.5 Adenosis

Adenosis of the breast is a proliferative lesion that is characterized by an increased number or size of glandular components mostly involving the lobular units. Various types of adenosis have been described, of which sclerosing adenosisn and microglandular adenosis merit detailed description (Lee K et al1996).

2.3.1.6Epithelial Hyperplasia

Epithelial hyperplasia (ductal or lobular type) is one of the most challenging FCCs to diagnose properly. Epithelial hyperplasia is the most common form of proliferative breast disease. It can be difficult to distinguish between ductal and lobular hyperplasias. In addition, it can also be difficult to distinguish between usual ductal or lobular Intraductal Papilloma and Papillomatosis Intraductal papilloma is a discrete benign tumor of the epithelium of mammary ducts. It can arise at any point in the ductal system and shows a predilection for the extreme ends of the ductal system: the lactiferous sinuses and the terminal ductules(Oyama T,et al,2004),

Papillomas are characterized by formation of epithelial fronds that have both the luminal epithelial and the outer myoepithelial cell layers, supported by a

fibrovascular stroma. The epithelial component can be subject to a spectrum of morphologic changes ranging from metaplasia to hyperplasia(figure6A,6B), atypical intraductal hyperplasia, and in situ carcinoma. The risk represented by the occurrence of such abnormalities in an otherwise benign papilloma is currently debated (MacGrogan G,et al,2003).

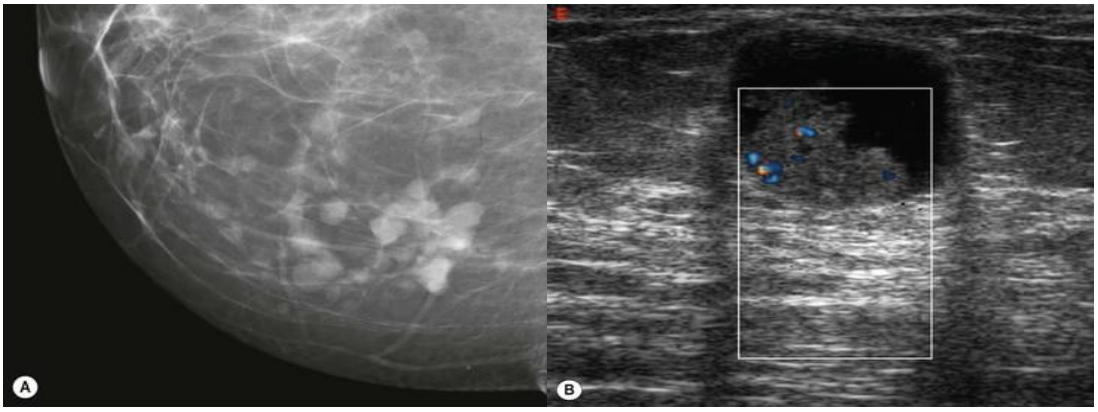


Fig (2.6) : Shows multiple small papilloma. (A) Papillomas are frequently well defined on mammography, although part of the mass may have an irregular or ill-defined contour. (B) On ultrasound, the presence of a filling defect within a cystic structure suggests the diagnosis. Colour Doppler can be useful for distinguishing debris within a cyst from a soft-tissue mass (.MacGrogan G,et al,2003).

2.3.1.6Fibroadenoma

Fibroadenoma is the most common lesion of the breast; it occurs in 25% of asymptomatic women (El-Wakeel H ,et al,2003),It is usually a disease of early reproductive life; the peak incidence is between the ages of 15 and 35 years. Conventionally regarded as a benign tumor of the breast, fibro adenoma is also thought to represent a group of hyperplastic breast lobules called “aberrations of normal development and involution(El-Wakeel H ,et al,2003; Hughes LE ,et al ,1987).

Fibroadenoma presents as a highly mobile, firm, nontender and often palpable breast mass(figure7). Although most frequently unilateral, in 20% of cases, multiple lesions occur

in the same breast or bilaterally. Fibroadenoma develops from the special stroma of the lobule. It has been postulated that the tumor might arise from bcl-2-positive mesenchymal cells in the breast, in a manner similar to that proposed for solitary fibrous tumors (Moore T,et al,2001).

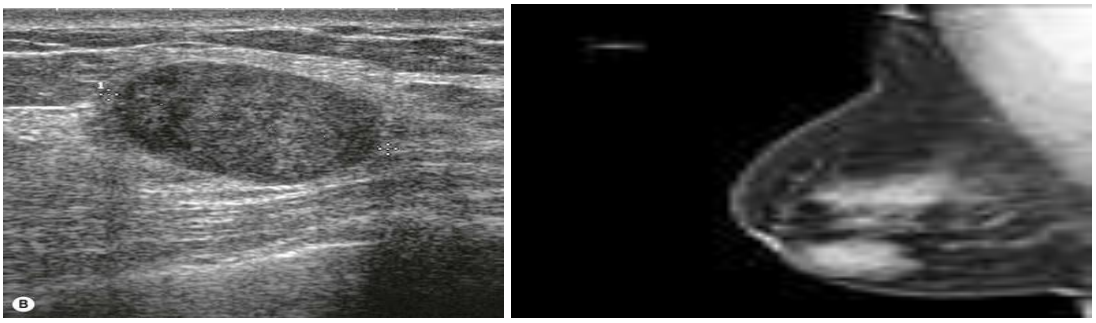


Fig (2.7) : Demonstrate fibroadenoma.(El-Wakeel H ,et al,2003)

2.3.1.7Lipoma :

Lipoma of the breast is a benign, usually solitary tumor composed of mature fat cells. It is occasionally difficult to distinguish lipoma from other conditions clinically, thus causing diagnostic and therapeutic challenges (Lanng C, et al 2004)

2.3.1.8Adenoma :

An adenoma is pure epithelial neoplasm of the breast. This lesion is divided into tubular, lactating, apocrine, ductal and so-called pleomorphic (i.e., benign mixed tumor adenoma) (Silverberg SG,et al 1997).

2.3.1.9Nipple adenoma, also known as florid papillomatosis of the nipple ducts or erosive adenomatosis, is a benign tumor of the ductal epithelium that often clinically mimics

Paget’s disease and pathologically may be misinterpreted as an adenocarcinoma. Typically, nipple adenoma presents as a discrete, palpable tumor of the papilla of

the nipple. Erosion of the nipple and nipple discharge are usually seen (Montemarano AD,et al 1995).

2.3.2Malignant Breast disease:

Is cancer that develops from breast tissue. signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, or a red scaly patch of skin (Breast Cancer Institute ". NCI.2014)

In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin (Saunders et al2009).

Risk factors for developing breast cancer include being female, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, older age, and family history About 5–10% of cases are due to genes inherited from a person's parents, including BRCA1 and BRCA2 among others. Breast cancer most commonly develops in cells from the lining of milk ducts and the lobules that supply the ducts with milk. Cancers developing from the ducts are known as ductal carcinomas, while those developing from lobules are known as lobular carcinomas(Breast Cancer". NCI.2014).

In addition, there are more than 18 other sub-types of breast cancer. Some cancers, such as ductal carcinoma in situ, develop from pre-invasive lesions (World Cancer Report 2014).The diagnosis of breast cancer is confirmed by taking a biopsy of the concerning lump. once the diagnosis is

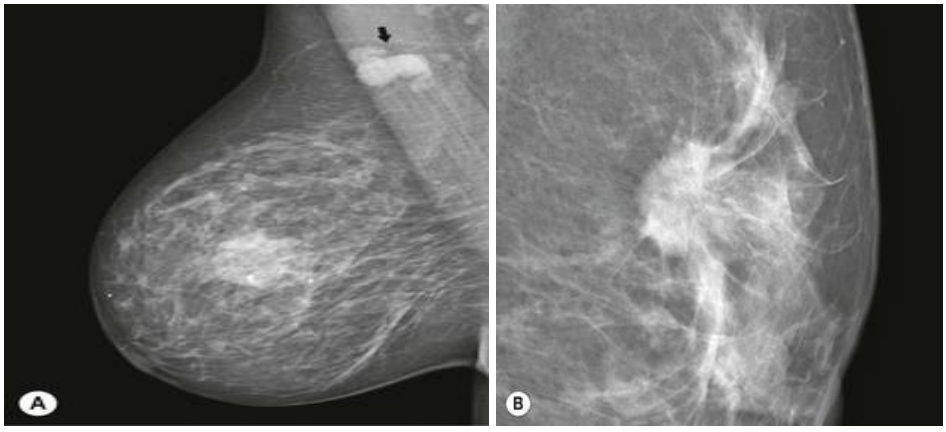
made, further tests are done to determine if the cancer has spread beyond the breast and which treatments it may respond to(Breast Cancer". NCI.2014)

Outcomes for breast cancer vary depending on the cancer type, extent of disease, and person's age. Survival rates in the developed world are high, with between 80% and 90% of those in England and the United States alive for at least 5 years(Breast Cancer Treatment PDQ®2014). In developing countries survival rates are poorer ,worldwide, breast cancer is the leading type of cancer in women, accounting for 25% of all cases. In 2012 it resulted in 1.68 million new cases and 522,000 deaths(World Cancer Report 2014).

It is more common in developed countries and is more than 100 times more common in women than in men. (National Cancer Institute. 2014).

2.3.2.1Ductal carcinoma :

In situ is the most common non-invasive breast cancer, in situ means 'in place' and refers to the fact that the cancer has not moved out of the duct and does not infiltrate the surrounding tissue. DCIS can progress to become invasive cancer(figure9A,9B)), but likelihood estimates vary of DCIS is diagnosed on mammography alone on the basis of microcalcifications.



Fig(2.8): Mammographic appearances of invasive carcinoma. Ill-defined and spiculate masses are typical of malignancy. (A) There is an ill-defined mass lying centrally in the right breast, containing some microcalcifications.(Breast Cancer Treatment (PDQ®) 2014)

2.3.2.2Inflammatory carcinoma :

Inflammatory carcinoma or mastitis carcinomatosa is a separate category of breast cancer and accounts for 1-5% of all breast cancers It is characterized by diffuse redness, peau d'orange and swelling of the breast, therefore it is mainly a clinical diagnosis

2.3.2.3Lobular carcinoma :

Invasive lobular carcinoma is the second most common type of breast cancer after invasive ductal carcinoma .Invasive lobular carcinomas tend to be more difficult to detect on mammography, because instead of forming a lump, the cancer cells typically spread to the surrounding connective tissue in a line formation(figure 2.9) (Bentzer et al.2016).

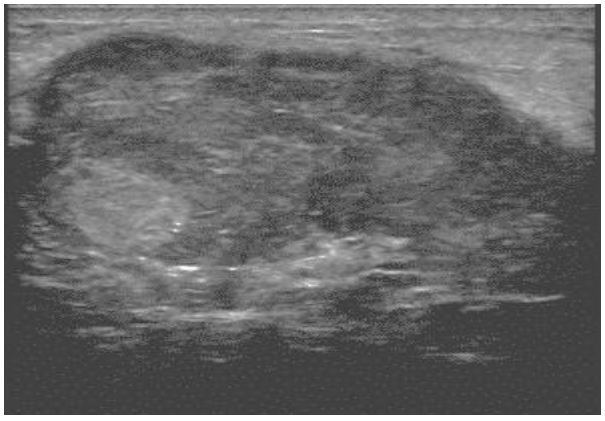


Fig (2.9) : Ultrasound image shows a large solid, heterogeneous mass, with hyperechoic, cystic areas intermixed and lobular margin. (Bentzer et al.2016)

2.3.2.4Triple negative breast cancer:

Approximately 15-20% of breast cancers are so-called triple negative and characterized by the absence of ER-, PR- and HER2-overexpression these tumors occur more often at a young age, are high-grade, and on presentation often substantial in size with metastases to the axillary lymph nodes. Triple negative tumors have a poorer prognosis with rapid recurrences, and frequent brain metastases (Bentzer et al 2016).

Breast cancer stage is the most important factor for prognosis. In general, the earlier the stage, the better the prognosis will be.

2.3.3Breast cancer staging:

Pathologic staging (the standard way to stage breast cancer) is based on a pathologist's study of the tumour tissue and any lymph nodes removed during surgery.

When needed, results from a health care provider's physical exam and/or tests like mammography may be used in addition to pathologic staging.

Ttable2.1:
BI-RADS Assessment Categories

Breast Imaging Reporting and Data System The table shows the assessment categories of Breast(Robin Smithuiset al 2016).

Final Assessment Categories			
Category		Management	Likelihood of cancer
0	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	n/a
1	Negative	Routine screening	Essentially 0%
2	Benign	Routine screening	Essentially 0%
3	Probably Benign	Short interval-follow-up (6 month) or continued	>0 % but ≤ 2%
4	Suspicious	Tissue diagnosis	4a. low suspicion for malignancy (>2% to ≤ 10%) 4b. moderate suspicion for malignancy (>10% to ≤ 50%) 4c. high suspicion for malignancy (>50% to <95%)
5	Highly suggestive of malignancy	Tissue diagnosis	≥95%
6	Known biopsy-proven	Surgical excision when clinical appropriate	n/a

2.2.4 previous study:

European Radiology March 2012, Volume 22, Issue 3, pp 539–544| Cite as One-to-one comparison between digital spot compression view and digital breast tomosynthesis Alberto Tagliafico et al, assessed diagnostic accuracy of DBT and spot compression view (DSCV) in 52 women who had a screening abnormality without calcification. Overall sensitivity was equal for both techniques (100%) for DBT and DSCV. Overall specificity was higher for DBT (100%) than for DSCV (94%).

American Journal of Roentgenology. 2013;200: 291-298. 10.2214/AJR.12.8881 Can Digital Breast Tomosynthesis Replace Conventional Diagnostic Mammography Views for Screening Recalls Without Calcifications? A Comparison Study in a Simulated Clinical Setting Kathleen R. et al Working on the same group of noncalcified findings recalled from screening mammography Kathleen RB et al, evaluated digital breast tomosynthesis (DBT) as an alternative to conventional diagnostic mammography in the workup of 146 women, with 158 of these abnormalities by three readers. For readers 1, 2, and 3, sensitivity and specificity of DBT for breast abnormalities were 100%, 100%, and 88% and 94%, 93%, and 89%, respectively.

Accuracy of Digital Breast Tomosynthesis for Depicting Breast Cancer Subgroups in a UK Retrospective Reading Study (TOMMY Trial) by gilbert et al, when they evaluated accuracy of digital breast tomosynthesis for depicting breast cancer subgroups in a UK retrospective reading study (TOMMY Trial) as they reported overall sensitivity of 87% for 2D mammography and 89% for 2D mammography plus DBT. They also

reported that addition of DBT increased the sensitivity of 2D mammography in women with dense breasts (86% for 2D mammography alone vs 93% for 2D mammography plus DBT) and the specificity of 2D mammography in all subgroups (58% for 2D mammography alone vs 69% for 2D mammography plus DBT).

International Journal if cancer research and treatment. March 2014 Accuracy of Mammography, Digital Breast Tomosynthesis, Ultrasound and MR Imaging in Preoperative Assessment of Breast Cancer by Giovanna mariscotti et al In their study to evaluate accuracy of mammography, DBT, US and MR imaging in preoperative assessment breast cancer, Mariscotti et al, presented DBT sensitivity of 90.7%

Diagnostic Mammographic Views for Evaluation of Noncalcified Breast Lesion Margarita L. alseries of 52 patients recalled from screening for noncalcified lesions, both tomosynthesis and diagnostic views were performed and evaluated by two radiologists (20). That study reported 100% sensitivity for both techniques and higher specificity for tomosynthesis than for supplemental views (100% vs 94%).

Assessing Radiologist Performance Using Combined Digital Mammography and Breast Tomosynthesis Compared with Digital Mammography Alone: Results of a Multicenter, Multireader Rafferty, et al Radiology. January 2013

Mammography is the only screening test that has been shown to reduce breast cancer-related mortality as Multiple randomized controlled trials have demonstrated that substantial reduction in breast cancer mortality can be realized through mammographic screening with the overall sensitivity of mammography is 70-90% .

However despite its clearly documented benefit, it is well recognized that mammography is imperfect. As many as 20%–30% of breast cancers will not be detected on a mammogram (6,7). One of the factors negatively affecting the performance of mammography is breast density. Mammographic sensitivity decreases with increasing parenchymal density On a two-dimensional mammographic projection, radiographically dense structures can be superimposed, potentially obscuring cancers. Conversely, these same overlapping structures can result in summation artifacts that mimic mammographic abnormalities prompting false-positive recalls

With the implementation of digital mammography, additional diagnostic accuracy can be achieved for specific subgroups of women, presumably from its superior ability to depict cancers in dense breast tissue.

European Radiology January 2010, Volume, Breast tomosynthesis in clinical practice: initial results Hendrik J, et al

in 2010, Hendrik J et al assessed the potential value of tomosynthesis in 513 women with an abnormal screening mammogram or with clinical symptoms. The sensitivity of both techniques for the detection of breast cancer was 92.9%, and the specificity of mammography and tomosynthesis was 86.1 and 84.4%, respectively.They found also 7% false-negative results.

Br J Radiol. 2016 Jun 2016 Apr 13.

Detection and characterization of breast lesions in a selective diagnostic population: diagnostic accuracy study for comparison between one-view digital breast tomosynthesis and two-view full-field digital mammography. breast lesions in 598 breasts of 319 diagnostic patients. DBT had higher overall sensitivity than FFDM (88.7% vs 80.7%, $p = 0.001$). Subgroup analyses showed that DBT had significantly higher sensitivity in assessing

dense breasts and invasive cancers than FFDM. The BI-RADS category assessment was significantly better for DBT than for FFDM. The differences between the two modalities in specificity (94.1% and 93.2% for FFDM and DBT) were not significant.

Ganime Dilek et al In a study specified for category 0 breast lesions, compare diagnostic performance and screening recall rates of digital breast tomosynthesis (DBT) and ultrasound (US) added to digital mammography (DM) in 216 women categorized as BI-RADS category 0 according to screening DM. For DBT, sensitivity, specificity, PPV, NPV and diagnostic accuracy were 97%, 82%, 48%, 99%, and 84%, whereas for US sensitivity, specificity, PPV, NPV and diagnostic accuracy were 93%, 79%, 47%, 98%, and 81%, respectively. AUC value was 0.89 and 0.86 for DBT and US.

Digital Breast Tomosynthesis: A New Diagnostic Method for Mass-Like Lesions in Dense BreastsLater in 2016, Tiantian Bian et al, compared the rates and accuracy of digital breast tomosynthesis (DBT) and 2D digital mammography (DM) for detecting and diagnosing mass-like lesions in dense breasts. They found significantly higher sensitivity, specificity, detection and diagnostic accuracy rates of DBT (68.1%, 95.2%, 84.3% and 82.3%, respectively) than that of DM (58.8% and 86.7%, 77.3% and 73.4%).

Diagnostic accuracy of digital breast tomosynthesis versus digital mammography for benign and malignant lesions in breasts: a meta-analysis

In 2014, Lei J et al Compared the results of seven studies involving 2,014 patients and 2,666 breast lesions with the gold standard (histological results) and they concluded DBT pooled sensitivity, specificity,

positive likelihood ratio and negative likelihood ratio of were 90.0% and 79.0%, 3.5 and 15% respectively.

Breast tomosynthesis and digital mammography: a comparison of diagnostic accuracy British journal of radiology · June 2012,

Svahn TM et al compared the diagnostic accuracy of both breast tomosynthesis and digital mammography and had average sensitivity of BT was higher than that for DM (90 vs ,79%) while the average false positive fraction was not significantly different (95% confidence interval of difference).

al In diagnostic settings, DBT improves work-up efficiency and the selection of patients recommended for biopsy, thereby reducing associated costs and additional imaging studies including additional mammographic views and unnecessary biopsies.

DBT offers potential advantages for evaluating masses, areas of architectural distortion, and asymmetries compared with those of conventional 2D mammographic images

Accuracy of classification of breast ultrasound findings based on criteria used for BI-RADS. Ultrasound Obstet Gynecol 2008.

Heinig J et al, Rahbar et al, Hong AS et al and Andrea S et al,we used these U/S features to characterize masses as malignant: irregular shape, hypoechoic, microlobulated / angular / spiculated margins, echogenic halo, non-parallel orientation, distal shadow, calcifications and penetrating vessels. U/S features that used to characterize masses as benign were: round or oval shape, circumscribed margins, non-hypoechoic, abrupt interface,

parallel orientation, with no distal shadow, no calcification and no penetrating vessels.

BI-RADS for sonography: positive and negative predictive values of sonographic features. AJR Am J Roentgenol 2005; These findings was comparable to those of Hong AS et al who founded high predictive value for malignancy include spiculated margin (86%), irregular shape (62%), and nonparallel orientation (69%). While for sonographic BI-RADS descriptors with highly predictive of benign lesions included circumscribed margin (90%), parallel orientation (78%), and oval shape (84%).

Benign versus malignant solid breast masses: US differentiation. Radiology 1999.

with Rahbar et al [14], as they found US features that most reliably characterize masses as benign were a round or oval shape (94%), circumscribed margins (91%), and a wider then tall (89%). They also found features that characterize masses as malignant included irregular shape (61), microlobulated (67%) or spiculated (67%) margins, and taller than wide (40%).

> Differential diagnosis of solid breast lesions: contribution of Doppler studies to mammography and gray scale imaging, J. Ultrasound Med. 2001. Ozdemir et al, neither morphologic nor spectral Doppler analysis proved to be successful on its own, but the information obtained could increase the diagnostic certainty of grayscale ultrasound and mammography,

Colour Doppler sonography of breast masses: a multiparameter analysis. Clin. Radiol. 1997;.

the study by Buadu et al who concluded that even the combination of color and spectral Doppler analysis does not appear to contribute significantly to the differentiation between benign and malignant breast lesions.

Kwak JY, et al. Power Doppler sonography evaluation of solid breast lesions and correlation with lymph node metastasis

These results with prospective clinical studies have evaluated the role of US in evaluation of breast masses, using BI-RADS category 4 as a cut-off point, the average sensitivities of US were > 95% (US range, 97.3-100%), whereas the average false-positive rates of US were approximately 60% (range, 56.8-68.2%).

Costantini M, Belli P, Ierardi C, Franceschini G, La Torre G, Bonomo L. Solid breast mass characterisation: use of the sonographic BI-RADS classification. Radiol Med 2007; 112: 877-94.

ACR indicates malignancy rates should be less than 2% in BI-RADS 3 lesions. In this study, none of the BI-RADS 3 lesions were defined as malignant (with an NPV of 100%), US sensitivity was 100 for both BI-RADS category 4 and 5 while false-positive rates were 96.4% for BI-RADS category 4, 5.5 % for BI-RADS category 5 and 65 % for combined BI-RADS category 4 and 5ACR statement of malignancy probability of BI-RADS 5 lesions as over 95%. It is also comparable with many studies presented rates for PPV of BI-RADS 5 lesions, ranging between 80 and 97%

Chapter Three

CHAPTER THREE
Material and Methods

3.1Setting and research design :

This is prospective hospital base study performed in the breast imaging facility at radiology department during the period from Mar 2015 to Sep 2018 at King Abdul-Aziz Specialist Hospital (KAASH), Taif city , Saudi Arabia.

3.2Study population:

A sample comprised of 200 Saudi females their age ranged from 25 years and above living in Taif city have had different types of breast lesions , this sample was collected when the patients attended radiology department for evaluation of their breast masses via mammography s screening , gray scale and colour Doppler ultrasound , the results of suspicious masses were confirmed with histopathology .

3.2.1Inclusion criteria :

i) Adults Saudi females, ages 25 and above.

3.2.2 Exclusion criteria :

Females who are not willing to participate in the study.

3.3Tool of data collection :

A structured questionnaire was designed for data collection by the researcher to perform the study based up on review of literature, questionnaire consists from four parts:

3.3.1First part contain:

Socio- demographic data (age, marital status and affected side, family history) .,

3.3.2Second part contain:

Ultrasound and Doppler result included information regarding the features of the breast: Shape (Round, Oval or Irregular), Margins (Circumscribed or Ill - defined), Width: AP ratio and Echogenicity (Hyperechoic, Hypoechoic or Isoechoic); on the basis of these four features a diagnosis was made. Ultrasound diagnosis was confirmed by FNAC or histopathology to categorize lesions as benign, malignant, or indeterminate.
U/S features that most reliably characterize masses as benign are: a round or oval shape, circumscribed margins, and a width to antero-posterior (AP) dimension ratio.

Features that characterize masses as malignant included irregular shape, microl-obulations, and width-to–AP dimension ratio . A few gently curving, circumscribed lobulations (macro-lobulations) are considered as benign features, whereas many small lobulations of 1-2 mm (micro-lobulation) are considered a malignant characteristic in a recent study.

3.3.3Third part contain :

Mammographic and tomosynthesis results.

3.3.4Fourth part :

Histopathology results.

3.4U/S technique and colour Doppler protocol:

Breast U/S requires a high frequency transducer (8-15) MHz .Ideally a wide footprint probe . A lower frequency transducer may be required for the larger attenuative breasts, inflammatory masses and the axilla . The use of a standoff may be required for nipple, superficial/or skin lesions . Low pulse repetition frequency (PRF) colour and spectral Doppler capabilities for assessing vascularity of lesions

3.4.1Patient Preparation:

Patient will be asked to undress from the waist up and to wear a gown during the examination , lie on his back on the examining table and asked to raise the arm above the head. After he positioned on the examination table, the radiologist (a physician specifically trained to supervise and interpret radiology examinations) or sonographer will apply a warm water-based gel to the area of the body being studied. The gel will help the transducer make secure contact with the body and eliminate air pockets between the transducer and the skin that can block the sound waves from passing into the body(Jorie Boulevard.et al2008).

3.4.2Imaging protocol:

The transducer is placed on the body and moved back and forth over the area of interest until the desired images are captured.

There is usually no discomfort from pressure as the transducer is pressed against the area being examined. However, if scanning is performed over an area of tenderness, the patient may feel pressure or minor pain from the transducer. Doppler sonography is performed using the same transducer. Once the imaging is complete, the clear ultrasound gel will be wiped off the skin. Any portions that are not wiped off will dry to a powder. The ultrasound gel does not stain or discolour clothing (Jorie Boulevard.et al2008).

3.4.3Ultrasound imaging technique:

She will be lying on her back on the examination bed in the ultrasound room, the upper body undressed, with one arm above your head on the pillow in a comfortable position. The sonographer will put a clear gel on your breast and the ultrasound transducer or probe (see ultrasound) will be slowly moved across the breast to show and identify the lesion on the ultrasound screen. Imaging was acquired using a LOGIQ 7 unit (GE Healthcare) with a 12-MHz linear transducer.

All examinations were interpreted by one of three radiologists experienced in breast imaging. The radiologist described the site (clock position and distance from the nipple), size, imaging characteristics of the lesions, BI-RADS assessments, and management.

3.4Tomosynthesis protocol:

Tomosynthesis is a digital method for performing high-resolution limited-angle tomography at radiographic dose levels Tomosynthesis is Food and Drug Administration (FDA) approved for use in breast cancer screening.

As of 2016 however it is unclear if its use in screening normal risk women is beneficial or harmful.

Digital breast tomosynthesis and DM were performed by one trained and dedicated technologist using a commercially available device (Selenia Dimensions System; Hologic, Bedford, MA, USA). The device consisted of a custom-designed high-power (mA) tungsten (W) anode X-ray tube and rhodium, silver, and aluminum X-ray filters. Different filters in DBT and DM imaging modes produce optimal X-ray spectra (20–49 kVp) based on the thickness/ composition of the breast using automatic exposure control. Different filters in DBT and DM imaging modes produce optimal X-ray spectra (20–49 kVp) based on the thickness/ composition of the breast using automatic exposure control. The image receptor was a 70-μm pixel pitch selenium direct capture detector. The X-ray tube moved over a 15° arc while the breast was compressed, taking a series of ultra-low dose mammograms. The projections were combined to create a full three dimensional-image set of the breast with 1-mm slices through the breast.

The DBT datasets were displayed using two high-resolution monitors (5 mega-pixels). The workstation allowed viewing the DBT images of both

breasts, one after the other (CC views and then MLO views of both breasts together)

3.5 Histopathology protocol :

Study is carried out by a pathologist experienced in the diagnosis of breast lesions. Malignant lesions are classified into seven categories according to histology: invasive ductal carcinomas not otherwise specified, medullary, apocrine, neuroendocrine carcinoma (A); tubular, mucinous, papillary carcinoma, cribriform carcinoma (B); metaplastic, anaplastic, undifferentiated high grade carcinoma (C); invasive lobular carcinoma (D); mixed ductal and lobular carcinoma (E); in situ carcinoma (F); and metastatic carcinoma (G), as proposed by Carey et al. For convenient statistical analysis, the lesions were allocated into three broad groups according to lesion hardness, whereby group 1 contained softer lesions (categories B, F, and G), group 2 contained harder lesions (categories A, D, and E), and group 3 comprised category C lesions. No group 3 lesions were included in this study because the five lesions assigned to this category were all non-mass lesions.

3.6.1Histopathology Protocol :

Patients underwent biopsy by percutaneous sample collection using a 14 gauge needle coupled with a semiautomatic core biopsy gun or vacuum-assisted breast biopsy using an 11 gauge needle (Eduardo de et al 2014).

1 -Fine Needle Aspiration Cytology / Biopsy in doubtful cases, post-operative follow up in operative cases .

2 -In cases of simple cysts and galactocele no histopathology confirmation was done. Aspiration of cyst was done to confirm .

3-No histopathology done in cases of normal ultra- sound findings and normal mammography in patients complaining of apparent mass felt on

clinical examination. Such patients refused to give consent for invasive histopathology study after normal reports and they were labelled as normal. Hence sensitivity and positive predictive value could not be obtained

Methods: Official permission to carry out.this study was obtained from the previously mentioned settings. Official permission to conduct the study was obtained from the research committee in King Abdul-Aziz Specialist Hospital (KAASH).Validity of tool will be reviewed by five experts from surgical nursing staff and content validity index will be calculated.

Fine-needle aspiration biopsy (FNAC/B).

Fine-needle aspiration cytology/biopsy (FNAC/B) of the breast is a well-established method to obtain fluid/tissue fragments and smears for preoperative diagnosis of breast lesions. FNAB is actually a safe and low-cost procedure that can avoid unnecessary surgery, differentiating with high accuracy benign and malignant lesions.

The procedure was performed by well-trained pathologists, using vigorous sampling and ultrasound guide fornonpalpable or hardly palpable lesions .FNAC is a diagnostic procedure that a pathologist or radiologist or surgeon uses a very thin needle usually (22- to 25) gauge connected to a vacuumed syringe to aspirate a small amount of tissue from the suspicious area. Its use to detect breast lesion became increasingly important from the 1980s as a diagnostic adjunct in the population based screening setting. FNAC is a safe, economical, effective, and accurate technique, but its efficacy largely depends on the experience of aspirators and pathologists .

3.7Statistical analysis:

Data coded, entered and analyzed using SPSS version 20. Descriptive statistical analysis was used to determine frequency distribution to obtained demographic variables in tables and graphs .

3.8Ethical considerations:

Ethical consideration: Research proposal was approved from Ethical Committee in both Radiology department, Taif University and (KAASH). There is no risk for study subjects during application of research. Ethical committee in (KAASH) was assured that the data of this research will not be reused without second permission

Chapter Four

CHAPTER FOUR

Results:

The mean age of the 200 patients was 43 years (ranging from 25-82 years), 97% were saudi while 3 % were non-saudi with 21% had +ve family history and 79 % did not (Graphs 1, 2 and 3 respectively).

Clinical presentation, side (right or left) and site of the lesion within the breast are listed in tables 1, 2 and 3 respectively.

227 indeterminate (Bi-RADS category 3) or suspicious breast lesions (Bi-RADS category 4 and 5) were found. Of these lesions, 74 were confirmed to be malignant (Table 4) and 153 had benign histopathological features (Table 5).

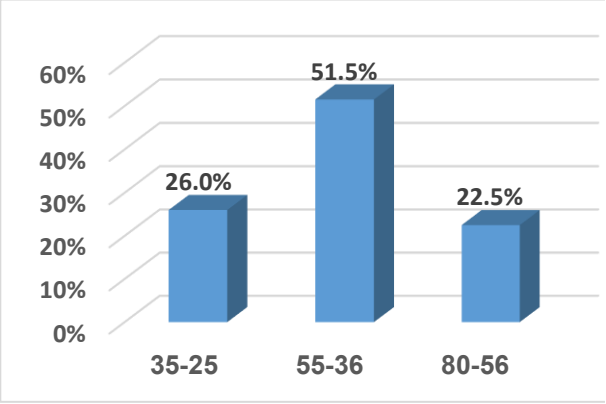
US description of the lesions including mass shape, echo pattern, margin, boundary, orientation, posterior acoustic features, and calcifications as well as their power doppler flow criteria (penetrating vessels) are demonstrated in Table 6.

DBT description of the lesions including mass shape, density, micro calcification, architectural distortion and nipple retraction are demonstrated in Table 7.

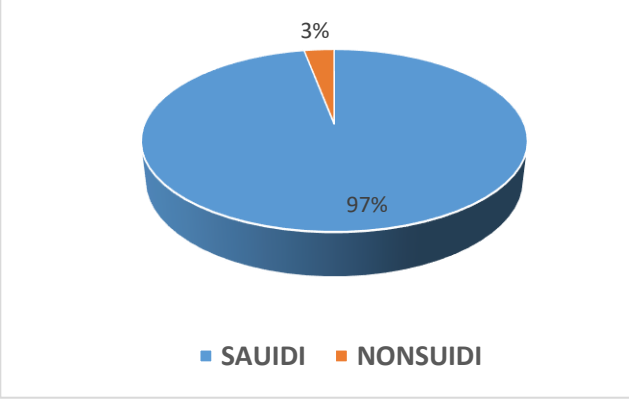
Regarding the probability of malignancy, it was determined by the radiologists according to Bi-RADS for all lesions. Number and incidence of malignant histological findings in relation to their estimated (BI-RADS) categories was compared to likelihood of malignancy of breast imaging reporting and data system (BI-RADS) categories for ultrasound and DBT in (Table 8).

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the greyscale US descriptors and power doppler criteria (penetrating vessels) as well as DBT descriptors for both malignant and benign lesions (Tables 9, 10, 11, 12 respectively).

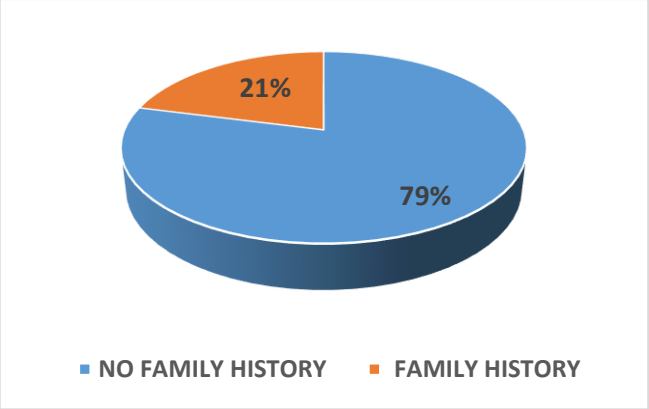
The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were also calculated for estimated Bi-RADS category of the lesions as an indicator of malignancy and combined lesions estimated Bi-RADS category and presence of penetrating vessels as an indicator of malignancy (Tables 13 & 14 respectively).



Graph 4.1: Age distribution among study sample. (n=200)



Graph 4.2: Nationality of patient among study sample. (n=200)



Graph 4.3: Family history of breast cancer among study sample.(n=200)

Table4. 1: Clinical finding among study sample. (n=200)

Clinical finding	Frequency	Percent
Palpable mass	105	52.5
Nipple discharge	14	7.0
Nipple retraction	8	4.0
Skin change	1	.5
Screening	24	12.0
Mass and nipple discharge	2	1.0
Mass, Nipple retraction and Skin changes	2	1.0
Nipple retraction and Nipple discharge	2	1.0
Mass, Skin changes and Nipple Discharge	1	.5
Mastalgia	41	20.5
Total	**200**	**100**

Table4. 2: Side of the breast lesion among study sample. (n=200)

Side	Frequency	Percent
Right	96	48.0
Left	104	52
Total	**200**	**100**

Table4. 3: Site of the lesion in the breast among study sample. (n=200)

Site	Frequency	Percent
Upper inner quadrant	50	25.0
Upper outer quadrant	59	29.5
Lower inner quadrant	19	9.5
Lower outer quadrant	15	7.5
Retroarolar	55	27.5

Table4. 4: Frequency distribution of histopathological patterns of the malignant breast lesions

Type of the lesion	Frequency	Percent
Invasive ductal carcinoma	48	64.8
Ductal carcinoma in situ	4	5.4
Invasive lobular carcinoma	10	13.5
Lobular carcinoma in situ	2	2.7
Mixed invasive ductal and lobular carcinoma	1	1.4
Tubular carcinoma	1	1.4
Mucinous carcinoma	2	2.7
Undifferentiated carcinoma	3	4
Inflammatory carcinoma	2	2.7
Malignant Phyllodes tumor.	1	1.4
Total	**74**	**100**

Table4. 5: Frequency distribution of histopathological patterns of the benign breast lesions.

Type of the lesion	Frequency		Percent
Fibroadenoma	64		41.8
Fibrocystic disease	49		32
Fibroadenoma with fibrocystic disease	16		10.4
Non-specific mastitis with breast abscess	5		3.3
Granulomatous mastitis	3		2
Tuberculosis mastitis	3		2
Lactating adenoma	2		1.3
Breast abscess	2		1.3
Duct papilloma	2		1.3
Benign phyllodes	2		1.3
Lipoma	1		0.7
Fat necrosis	4		2.6
Total	**153**		**100**

Table 4. 6: Frequency of Benign and Malignant Masses for grey scale US Descriptors and Power Doppler flow criteria. A percentage of 227 masses, B. percentage of benign lesions among total number of masses with given descriptor and C. Percentage of malignant lesions among total number of masses with given descriptor.

US Descriptor	Number	A	Benign	B	Malignant	C
						Shape
Oval	127	56	117	92	10	8
Round	11	5	9	82	2	18
Irregular	89	39	27	30	62	70
						Echogenicity
Non-hypoechoic	84	37	33	39	51	61
Hypoechoic	143	63	89	62	54	38
						Margin
Circumscribed	110	48	101	92	9	8
Indistinct	54	24	29	54	25	46
Angular	25	11	10	40	15	60
Microlobulated	29	13	12	41	17	59
Speculated	9	4	1	11	8	89
						Boundary
Abrupt interface	155	68	61	39	94	61
Echogenic halo	74	32	46	62	28	38
						Orientation
Parallel	170	75	134	79	36	21
Not parallel	57	25	19	33	38	67
						Posterior acoustic features
Normal	93	41	81	87	12	13
Enhancement	44	19	36	82	8	18
Shadowing	77	34	30	39	47	61
Mixed	13	6	6	46	7	54
						Microcalcifications
No	199	88	150	75	49	25
Yes	28	12	3	11	25	89
						Power doppler flow criteria (penetrating vessels)
No	181	80	141	78	40	22
Yes	46	20	12	26	34	74

Table4. 7: Frequency of Benign and Malignant Masses for Digital breast Tomosynthesis criteria. A percentage of 227 masses, B. percentage of benign lesions among total number of masses with given descriptor and C. Percentage of malignant lesions among total number of masses with given descriptor.

DBT Descriptor		Nu	A	Benign	B	Malignant	C
Mass	**Shape**						
	Oval	43	18	37	81	5	18
	Round	62	27	55	89	7	11
	Irregular	122	53	47	39	75	61
							Density
	High	135	59	98	59	55	41
	Medium	85	37	29	54	12	46
	Low	12	6	12	100	0	0
							Architectural Distortion
No		174	76	136	78	37	21
Yes		53	23	28	53	25	47
							Nipple Retraction
No		174	76	138	80	36	20
Yes		54	24	13	39	31	61
							Micro calcification
No		125	55	100	80	25	20
Monomorphic, fine		61	27	53	87	13	13
Pleomorphic, Amorphous		41	18	11	27	30	73

Table 4.8: Number and incidence of malignant histological findings in relation to their estimated (BI-RADS) categories was compared to likelihood of malignancy of breast imaging reporting and data system (BI-RADS) categories for ultrasound and DBT

Category	Number	Percentage	Number of malignant lesions at histological examination	Percentage	Expected rate of malignancy after US BI-RADS categorization (%)
3	15	6.7	0	0	< 2
4	139	61.5	5	3.6	3–94
5	73	31.8	69	94.5	> 94
Total	227	100	74	100	

Table4. 9: Statistical analysis of grey scale US descriptors and power doppler flow criteria for malignant lesions

Us descriptors	Sensitivity	Specificity	PPV	NPV
Irregular shape	83.8	82.4	69.7	91.3
Microlobulated/angular/spiculated margins	81.6	81.5	63.5	91.8
Hypoechoic	51.4	27	37.8	39.3
Echogenic halo interface	23	57	37.8	39.4
Non-Parallel orientation	51.4	87.6	66.7	78.8
Distal shadow	70.1	79.6	61	85.4
Calcification	33.8	98	89.3	75.4
Penetrating vessels	45.9	92.2	73.9	77.9

Table 4.10: Statistical analysis of grey scale US descriptors and power doppler flow criteria for benign lesions

Us descriptors	Sensitivity	Specificity	PPV	NPV
Round or oval shape	82.4	83.8	91.3	69.7
Circumscribed margins	81.5	81.6	91.8	63.5
Non-hypoechoic	27	51.4	39.3	37.8
Abrupt interface	57	23	39.4	37.8
Parallel orientation	87.6	51.4	78.8	66.7
Distal shadow	79.6	70.1	85.4	61
Calcification	98	33.8	75.4	89.3
Penetrating vessels	92.2	45.9	77.9	73.9

Table4. 11: Statistical analysis of DBT descriptors criteria for malignant lesions

DBT descriptors		Sensitivity	Specificity	PPV	NPV
Mass	**Irregular shape**	88.2	66,1	88.4	61.4
	High Density	88.7	46.4	87.6	35.9
Architectural Distortion		40.3	81	81.5	39.6
Nipple Retraction		46.6	85.7	78.9	58.3
Suspicious Micro calcification		44.1	93.2	80.1	73.1

Table4. 12: Statistical analysis of DBT descriptors criteria for benign lesions

DBT descriptors		Sensitivity	Specificity	PPV	NPV
Mass	**Oval ,round shape**	**66.1**	**86.2**	**61.4**	**88.4**
	Non-High Density	**46.4**	**88.7**	**35.9**	**87.6**
No Architectural Distortion		**81**	**40.3**	**39.6**	**81.5**
No Nipple Retraction		**85,7**	**46.6**	**58.3**	**78.9**
No suspicious Micro calcification		**93.2**	**44.1**	**73.1**	**80.1**

Table 4.13: Statistical analysis of the lesions estimated Bi-RADS category as an indicator of malignancy

Category	Sensitivity	Specificity	PPV	NPV
4+ Penetrating vessels	**49.4**	**51.7**	**21**	**79.6**
5+ Penetrating vessels	**72**	**90.6**	**86.6**	**79.6**
4 and 5+ Penetrating vessels	**73**	**51**	**41.9**	**79.6**

Table4. 14: Statistical analysis of combined lesions estimated Bi-RADS category and presence of penetrating vessels as indicators of malignancy

Category	Sensitivity	Specificity	PPV	NPV
4	**100**	**10**	**3.6**	**100**
5	**100**	**78.9**	**94.5**	**100**
4 and 5	**100**	**10**	**35**	**100**

Chapter Five

CHAPTER FIVE
DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

The current study aims to highlight the role of combined breast ultrasound and tomosynthesis imaging in detection and characterization of breast lesions. 200 samples of patients who transferred for imaging department for breast imaging were collected. Their age was between 25 and 82 years and most of sample was in age group of 36-55 years (Graph1).

According to the American Cancer Society, about 1 out of 8 invasive breast cancers develop in women younger than 45, about 2 out of 3 invasive breast cancers are found in women 55 or less so the current result is not a way from the results carried by American Cancer Society. In fact the aging process is the biggest risk factor for breast cancer because of longer their live so there are more chance for appearance.

Among the sample of this study around 21% had family history of malignant breast lesion(graph 4.3).

A strong family history of breast cancer is linked to having an abnormal gene associated with a high risk of breast cancer, such as the BRCA1 or BRCA2 gene also, an abnormal CHEK2 gene may play a role in developing breast cancer (Laufey T,Shin,Bernardi D)

The most clinical findings in our sample was palpable mass (52%)(table 4.1), and the less frequent finding was skin change (0.5%), while during study carried by Babatunde A Ayoadein Nigeria the commonest symptoms were, breast lump in 111 patients, (91.7%) and breast pain in 28 patients (23.1%).

Through our sample (n=200) 52% of lesion seen in the left breast(table4.2). Many studies have shown that unilateral breast cancer is more frequent in the left breast than in the right. This has been investigated in the Icelandic Cancer Registry. Information on all but 18 female breast cancer cases diagnosed in the forty-year-period from 1948 to 1987, a total of 2139 cases, was used. Of these 2011 were unilateral, 1069 were in the left breast, an excess of 13%. Primary breast cancer in both breasts was diagnosed in 81 women, 35 in the left breast first, and 46 in the right breast.

In the current study 52% have palpable mass, compared to literature (Lourenc AP, Skaane P, Ho JM) it was somewhat agreeing. A breast lump may or may not be noticeable to the patient; normal breast tissue can be quite lumpy in some women and some lumps can be small or located deep in the breast. Special tests such as a mammogram often detect breast lumps that cannot be felt. Over 90% of breast lumps are caused by benign breast disease, a range of non-cancerous conditions.

Mammography is the only screening test that has been shown to reduce breast cancer-related mortality as Multiple randomized controlled trials have demonstrated that substantial reduction in breast cancer mortality can be realized through mammographic screening with the overall sensitivity of mammography is 70-90% (Sun Ah Kim, Berry DA, Hellquist BN, Tabár L). One of the factors negatively affecting the performance of mammography is breast density. Mammographic sensitivity decreases with increasing parenchymal density (Pisano ED Carney PA)], and sensitivity is as low as 30-48% in women with dense breast tissue (Mandelson MT,Kerlikowske K).

On a two-dimensional mammographic projection, radiographically dense structures can be superimposed, potentially obscuring cancers. Conversely, these same overlapping structures can result in summation

artifacts that mimic mammographic abnormalities prompting false-positive recalls

With the implementation of digital mammography, additional diagnostic accuracy can be achieved for specific subgroups of women, presumably from its superior ability to depict cancers in dense breast tissue (Pisano ED). Recent technical developments in DM have enabled the introduction of digital breast tomosynthesis (DBT) as a clinical imaging modality that permits individual planes of the breast to be visualized while reducing the impact from overlapping tissue. Unlike conventional digital mammography, in which each image is created from a single x-ray exposure, tomosynthesis images are reconstructed from a series of low-dose exposures as the x-ray source moves in an arc or linear trajectory above the breast. The resultant imaging data set minimizes the effect of overlapping structures, affording tomosynthesis the potential to enhance both the sensitivity and specificity of mammographic imaging (Sun Ah Kim)

In diagnostic settings, DBT improves work-up efficiency and the selection of patients recommended for biopsy, thereby reducing associated costs and additional imaging studies including additional mammographic views and unnecessary biopsies Tagliafico A et al.

The presence of the standard mammogram facilitates comparison with prior examinations and provides a comprehensive view of distributional features (particularly for calcifications) while the addition of tomosynthesis minimizes the effect of tissue overlap and allows better visualization of noncalcification features. Thus the relative strengths of the two modalities are retained with the combined approach; however, the addition of tomosynthesis to the standard mammogram represents additional radiation exposure to the patient.

Investigational efforts are underway to replace the standard mammogram with a mammogram synthesized from the tomosynthesis images to reduce the dose(Elizabeth A).

US is an established, diagnostic tool that has been used to evaluate specific areas of abnormality discovered on either a clinical examination or mammography in order to characterize breast lesions and to differentiate between benign and malignant lesions

Previous prospective clinical studies have demonstrated that appropriate use of US as an adjunct to mammography improves sensitivity and specificity of breast cancer diagnosis, particularly in women with dense breasts and in younger women.

This is an important issue, as dense breast tissue is very common, the interval cancer rate is highly increased in this group and, furthermore, dense breast tissue is itself a marker of increased risk of breast cancer in the order of 4–6-fold .

With the increasing use of US for breast lesions, ACR described BIRADS lexicon classification for US in 2003 to provide a common language and determine a more accurate description for clinician. It is considered as a standard guideline that is widely used in the evaluation and categorization of breast lesions (as benign, probably benign, suspicious and highly suspicious of malignancy).

According to the ACR BI-RADS criteria, the presence of a single malignant feature in a breast lesion renders it a BI-RADS 4 or 5 lesions (i.e. suspicious or highly suspicious of malignancy).

The growth of a breast cancer is closely associated with abnormal new blood vessel formation or angiogenesis as the cancer cells stimulate the development of abnormal new vessels. The presence of intratumoural

vessels was significantly associated with malignancy and according to Stuhrmann M et al , the presence of intratumoural vessels can be used to determine the prognosis of breast cancer as well as the therapeutic approach for it.

PDUS was selected over colour doppler US to evaluate the vascular pattern of lesions, as the former has a higher sensitivity in detecting flow in solid breast lesions, particularly if small vessels and low-velocity blood flow are involved.

Also, since PDUS measures the amplitude of blood flow, it is angle-independent and avoids aliasing artefacts.

In our study, most of the lesions were suspicious or highly suspicious of malignancy (exhibiting one or more suspicious sonographic features) except for 15 lesions were not suspicious but biopsied per our institute standards being either in a patient with past history of cancer breast or larger than 2.5 cm diameter when first diagnosed or for patient psychological and mental relief.

In this study, none of the BI-RADS 3 lesions were defined as malignant (with an NPV of 100%). Starting at BI-RADS category 4, both DBT and US sensitivity was 100 for both BI-RADS category 4 and 5 while false-positive rates were 96.4% for BI-RADS category 4, 5.5 % for BI-RADS category 5 and 65 % for combined BI-RADS category 4 and 5.

These results agree with previous prospective clinical studies have evaluated the role of DBT in detection and characterization of breast lesions like Sun Ah Kim, et al, who demonstrated DBT sensitivity of 97.3% and specificity of 44.7%.

Earlier in 2010, Hendrik J et al, assessed the potential value of tomosynthesis in 513 women with an abnormal screening mammogram or

with clinical symptoms. The sensitivity of both techniques for the detection of breast cancer was 92.9%, and the specificity of mammography and tomosynthesis was 86.1 and 84.4%, respectively.They found also 7% false-negative results.

In another series of 52 patients recalled from screening for noncalcified lesions, both tomosynthesis and diagnostic views were performed and evaluated by two radiologists Teertstra HJ et al. That study reported 100% sensitivity for both techniques and higher specificity for tomosynthesis than for supplemental views (100% vs 94%).

In their study to evaluate accuracy of mammography, DBT, US and MR imaging in preoperative assessment of breast cancer, Mariscotti et al, presented DBT sensitivity of 90.7%.

Alberto Tagliafico et al, assessed diagnostic accuracy of DBT and spot compression view (DSCV) in 52 women who had a screening abnormality without calcification. Overall sensitivity was equal for both techniques (100%) for DBT and DSCV. Overall specificity was higher for DBT (100%) than for DSCV (94%).

Working on the same group of noncalcified findings recalled from screening mammography Kathleen RB et al, evaluated digital breast tomosynthesis (DBT) as an alternative to conventional diagnostic mammography in the workup of 146 women, with 158 of these abnormalities by three readers. For readers 1, 2, and 3, sensitivity and specificity of DBT for breast abnormalities were 100%, 100%, and 88% and 94%, 93%, and 89%, respectively.

Similar results was found by gilbert et al, when they evaluated accuracy of digital breast tomosynthesis for depicting breast cancer subgroups in a UK retrospective reading study (TOMMY Trial) as they reported overall

sensitivity of 87% for 2D mammography and 89% for 2D mammography plus DBT. They also reported that addition of DBT increased the sensitivity of 2D mammography in women with dense breasts (86% for 2D mammography alone vs 93% for 2D mammography plus DBT) and the specificity of 2D mammography in all subgroups (58% for 2D mammography alone vs 69% for 2D mammography plus DBT).

Svahn TM et al compared the diagnostic accuracy of both breast tomosynthesis and digital mammography and had average sensitivity of BT was higher than that for DM (90 vs ,79%) while the average false positive fraction was not significantly different (95% confidence interval of difference).

In 2014, Lei J et al Compared the results of seven studies involving 2,014 patients and 2,666 breast lesions with the gold standard (histological results) and they concluded DBT pooled sensitivity, specificity, positive ratio and negative ratio of were 90.0% and 79.0%, 3.5 and 15% respectively.

Later in 2016, Tiantian Bian et al, compared the rates and accuracy of digital breast tomosynthesis (DBT) and 2D digital mammography (DM) for detecting and diagnosing mass-like lesions in dense breasts. They found significantly higher sensitivity, specificity, detection and diagnostic accuracy rates of DBT (68.1%, 95.2%, 84.3% and 82.3%, respectively) than that of DM (58.8% and 86.7%, 77.3% and 73.4%).

Again in 2016, Chae EY et al compared the performance of one-view digital breast tomosynthesis (DBT) and two-view full-field digital mammography (FFDM) in the detection and characterization of breast lesions in 598 breasts of 319 diagnostic patients. DBT had higher overall sensitivity than FFDM (88.7% vs 80.7%, $p = 0.001$). Subgroup analyses showed that DBT had significantly higher sensitivity in assessing dense

breasts and invasive cancers than FFDM. The BI-RADS category assessment was significantly better for DBT than for FFDM. The differences between the two modalities in specificity (94.1% and 93.2% for FFDM and DBT) were not significant.

In a study specified for category 0 breast lesions, Ganime Dilek Emlik et al, compare diagnostic performance and screening recall rates of digital breast tomosynthesis (DBT) and ultrasound (US) added to digital mammography (DM) in 216 women categorized as BI-RADS category 0 according to screening DM. For DBT, sensitivity, specificity, PPV, NPV and diagnostic accuracy were 97%, 82%, 48%, 99%, and 84%, whereas for US sensitivity, specificity, PPV, NPV and diagnostic accuracy were 93%, 79%, 47%, 98%, and 81%, respectively. AUC value was 0.89 and 0.86 for DBT and US.

Recently, Hawley JR et al evaluated combined 2D mammography, DBT, and US at palpable sites where two breast imagers reviewed blinded a total of 229 sites in 188 patients with combined 2D mammograms and DBT examinations performed for palpable complaints. Their sensitivities for 2D, DBT, and US were 100.0%, 94.4%, and 100.0%. The negative predictive value, when combined with US, was 100% for both. The sensitivity and the specificity for both benign and malignant findings with 2D and DBT were 70.5% versus 75.4% and 95.3% versus 99.1%.

In this study, DBT allowed the detection of a greater number lesions and a better morphological analysis of masses and architectural distortions than DM, there was no need for operator training as the breast is positioned just like a conventional mammography or for the radiologist as he continues to perform diagnosis from images with mammograms features, in fact all readers found it easier. Additional benefit we noted, DBT helped precisely

localize a breast lesion visible only on one standard mammographic projection for further evaluation/biopsy. These benefits were stated also by many authors (Yamin Cohen , Chae EY, Kathleen R).

Following Heinig J et al, Rahbar et al, Hong AS et al and Andrea S et al ,we used these U/S features to characterize masses as malignant: irregular shape, hypoechoic, microlobulated / angular / spiculated margins, echogenic halo, non-parallel orientation, distal shadow, calcifications and penetrating vessels. U/S features that used to characterize masses as benign were: round or oval shape, circumscribed margins, non-hypoechoic, abrupt interface, parallel orientation, with no distal shadow, no calcification and no penetrating vessels.

The study was not include lesions with indistinct margin (29 benign and 25 malignant) and those with mixed posterior acoustic features (6 benign and 7 malignant) as both did not show significant difference between benign and malignant lesions. Our finding that US grey scale descriptors of shape, margin, orientation, posterior acoustic features and calcification can be used to predict whether the lesions were benign or malignant while echogenicity and boundary didn't show significant role.

This was concluded from high PPV for malignancy for irregular shape, microlobulated /angular/spiculated margins, non-parallel orientation, distal shadow and presence of calcifications (69.7, 63.5, 66.7, 61 and 89.3 respectively) and relatively low PPV for malignancy for low echogenicity and presence of echogenic halo (37.8 for both). For benign lesions these sonographic BI-RADS descriptors had a high predictively; round or oval shape, circumscribed margins, parallel orientation, no distal shadow and no calcification (91.3, 91.8, 78.8, 85.4 and 75.4 respectively) and relatively low

PPV for benignity for non-hypochogenicity and presence abrupt interface (39.3 and 39.4 respectively).

These findings was comparable to those of Hong AS et al , who founded high predictive value for malignancy include spiculated margin (86%), irregular shape (62%), and nonparallel orientation (69%). While for sonographic BI-RADS descriptors with highly predictive of benign lesions included circumscribed margin (90%), parallel orientation (78%), and oval shape (84%).

Study findings also agreed with Rahbar et al, as they found US features that most reliably characterize masses as benign were a round or oval shape (94%), circumscribed margins (91%), and a wider then tall (89%). They also found features that characterize masses as malignant included irregular shape (61), microlobulated (67%) or spiculated (67%) margins, and taller than wide (40%).

But current study disagrees with Heinig J et al, regarding lesion orientation as they did not find the non-parallel orientation feature to be significantly associated with malignancy in contrast to Gokalp et al, and Stavros AT et al, who stated that non parallel orientation shown to correlate well with malignancy while parallel orientation is associated with benignity.

They relied this to small sample size of their study or the size of the lesions examined, which were mostly > 2 cm.

Regarding penetrating vessels, we found a significant difference between malignant and benign lesions as presence of penetrating vessels had a high PPV, 73.9 for malignancy while their absence had a high PPV, 77.9 for benignity. Our findings were comparable to those described by Raza and Baum, who found that the sensitivity, specificity, PPV and NPV of using

penetrating vessels to predict malignancy were 68%, 95%, 85% and 88%, respectively.

Such findings are confirmed also by Studies conducted by Gokalp et al, Kwak et al and Lee et al, who found vascular patterns of the lesions, as seen on PDUS, correlated with the histopathology results in their study, with high specificity and NPV.However, in the study of Ozdemir et al, neither morphologic nor spectral Doppler analysis proved to be successful on its own, but the information obtained could increase the diagnostic certainty of grayscale ultrasound and mammography. Similar results were obtained in the study by Buadu et al who concluded that even the combination of color and spectral Doppler analysis does not appear to contribute significantly to the differentiation between benign and malignant breast lesions.

For BI-RADS category correlation with malignancy, ACR indicates malignancy rates should be less than 2% in BI-RADS 3 lesions. In this study, none of the BI-RADS 3 lesions were defined as malignant (with an NPV of 100%), US sensitivity was 100 for both BI-RADS category 4 and 5 while false-positive rates were 96.4% for BI-RADS category 4, 5.5 % for BI-RADS category 5 and 65 % for combined BI-RADS category 4 and 5.

These results agree with previous prospective clinical studies have evaluated the role of US in evaluation of breast masses, using BI-RADS category 4 as a cut-off point, the average sensitivities of US were > 95% (US range, 97.3-100%), whereas the average false-positive rates of US were approximately 60% (range, 56.8-68.2%).

Sensitivity and NPVs in our study (100% and 100%) were similar to Zengin B et al and Graf et al and little better when compared to other studies. Park et al reported a sensitivity of 96-100%, and NPV of 95-100% in their study. In a study conducted by Lee et al,sensitivity was reported as 97-98% and

NPV as 94-96%. Constantini et al reported their sensitivity was 98.2% and NPV was 95.2% in the study. In their study, Stavroset al reported a sensitivity of 98.4% and NPV of 99.5%. Lai et al reported a lower degree of sensivity and NPV as 91-95% and 81-93%, respectively.

Although the false positive results were high in our study, there are several studies in the literature in accordance with our findings. Zengin B et al had (20.7% and 30.3) specificity results, Park et al[43] reported their specificity results ranged between 8 and 43%. This level was 26-40% in the study of Lee et al and 45-77% in the study of Lai et al.

In our study, PPVs was 35%. This parameter was found to be ranging between 24.7 and 27.2% in Zengin B et al study, and to be 30-40%; 38%; and 72% in the studies of Stavros et al; Park et al; and Constantini et al, respectively.

In our study, PPVs was 3.6% for BI-RADS 4 lesions. These results are comparable with ACR statement of malignancy probability of BI-RADS 4 lesions as between 3-94%. However our results are lower than those of Yoon et al, Heining et al, and Wiratkapun et al studies who reported PPVs of 18.6%, 17%, 16.2%, 21% respectively.

This could be explained by increased PPV with increased prevalence of malignancy and in our study, we encountered lower malignancy rate, 32.6% compared to higher malignancy rates of studies reported higher PPV results as it was 51.3%, 57.5%, and 53.3% in the studies of Lee et al, Constantini et al, and Lai et al, respectively.

In this study, PPVs was 94.5% for BI-RADS 5 lesions. These results are comparable with ACR statement of malignancy probability of BI-RADS 5 lesions as over 95%. It is also comparable with many studies presented rates for PPV of BI-RADS 5 lesions, ranging between 80 and 97%. However

other studies reported PPV of BI-RADS 5 lesions lower than stated by ACR, like Tan et al (84%), Zengin B et al (66.7-84.6%), Raza et al (88.8%) and Hamy et al (78.7%). Except Tan et al, the other studies who reported PPV of BI-RADS 5 lesions lower than stated by ACR, were conducted on non-palpable breast masses, so this might be one of the reasons for the lower rates in these studies.

Combining both grey scale US and PDUS method, we obtained a much higher diagnostic accuracy of PPV and specificity for combined BI-RADS 4 category and PDUS method (21% and 51.7%) than that obtained by BI-RADS 4 category alone (3.6% and 10%).

Also, there was higher diagnostic accuracy of PPV and specificity for combined BI-RADS 4,5 categories and PDUS method (41.9% and 51%) than that obtained by BI-RADS 4,5 categories alone (35% and 10%).

In the same time, diagnostic accuracy of PPV and specificity for combined BI-RADS 5 category and PDUS method (86.6% and 90.6%) were comparable with that obtained by BI-RADS 5 category alone (94.5% and 78.9%).

Regarding this point we agree with that reported by Kwak et al, Gokalp et al and Ibrahim R et al.

Our results indicate that the diagnostic performance of combined DBT and US for characterizing breast lesions provides interpretive advantages however, the main problem of ultrasound is the dependence on different variables and being operator dependent. In this study 5 lesions were not seen in US initially, after revising mammography images, they were detected in the second look US of a particular area of the breast detected by mammography.

5.2CONCLUSION:

Tomosynthesis offers the dual benefit of improved diagnostic accuracy particularly in younger women with dense breasts and significant reduction in false-positive recall rate thereby avoiding unnecessary additional testing and decreasing attendant anxiety, inconvenience, and cost for women.

Breast US is a useful diagnostic tool in breast cancer detection and can be used to characterize breast lesions. The vascular flow patterns of breast lesions on PDUS provides additional benefit for the differentiation of benign and malignant breast lesions.

ACR BI-RADS lexicon provides standardized terminology to facilitate accurate and consistent breast sonography reporting and can be helpful in distinguishing benign from malignant breast masses.

Utilizing technologic advances can eliminate operator dependence-related mistakes.

5.3. RECOMMENDATION

- Application of a new protocol for all patient who refer to radiology department for breast imaging and with age more than 36 combined the ultrasound and DBT as first step to recognize any breast lesion to increase the early detection of malignant breast lesion so as to safe women life
- Uses the Doppler ultrasound to increase the sensitivity to facilitate differentiate the breast lesion
- More research studies about the new DBT to improve the benefits and effects of it.
- larger prospective studies to determine which modality and/or combination of modalities is optimal for screening depending

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Appendices

APPENDIX(A)
DATA COLLECTION SHEET

Age	F.H	MAR	CLINCALLY			
			mass	Nipple D.RETRA	SKIN CHANGE	AXillary EVALUTION

Ultrasound

BREAST COMPOSITION	MASS							
A B C	SHAPE	SITE	ORIENTATION	CALCFICATION	MARGIN		ECHO PATTERN	Vascurity
					Circum-scribed	Not		
	Oval Round	UIQ UOQ LIQ LOQ AX TAIL ,R O	Parallel Non parallel	Inter mass Out mass Intra duct		Angular speculated macrolobulation indistinct	ANECHOIC HEPERECHOIC HYPOEHOIC COMPLEX SOLID,CYSTIC HETROGENOUS	A vascular Internal rim

BREAST COMPOSITION			MASS							
C	B	A	SHAPE	SITE	ORIENTATION	CALCFICATION	MARGIN		ECHO PATTERN	Vascurity
							Circumscribed	Not		

Associated feature		
Duct changes	Skin thickening	Skin refraction

Mammographic and tomosynthesis

Breast composition	Mass			Architectural distortion	calcification		
	Shape	Density	Margin	Yes no	distribution	Sus	benign
A B C D	irregular round oval	Fat Low Equal High	Circumscribed Obscured Microlobulated Indistinct Speculated		Diffuse Segmental Linear Group	Amorphous Corse hetr Fine linear Linear branching	

Mammographic and Tomosynthesis

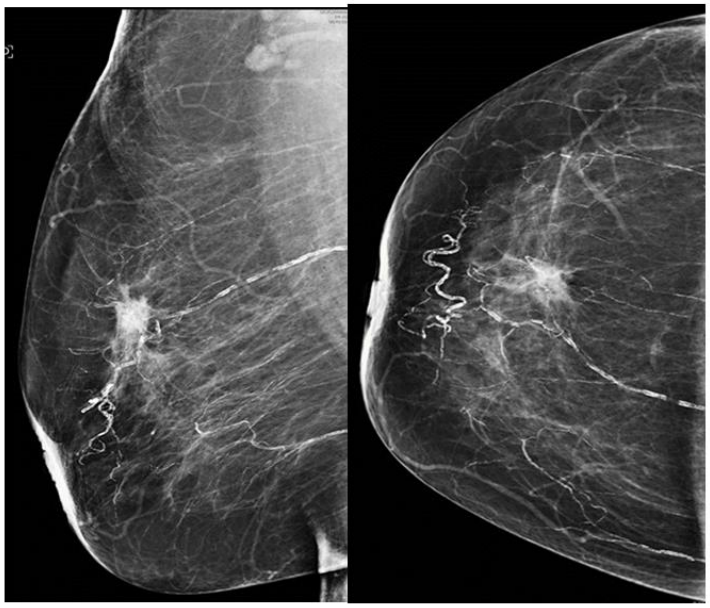
BREAST COMPOSITION	MASS			Asymmetry	Calcification	
	SHAPE	Density	Margin		morphology	Distribution
					Sus Benign	

Nipple retraction	Skin retraction	Skin thickening	Other

HISTOPATHOLOGY RESULT

APPENDIX(B)
CASES

case 1



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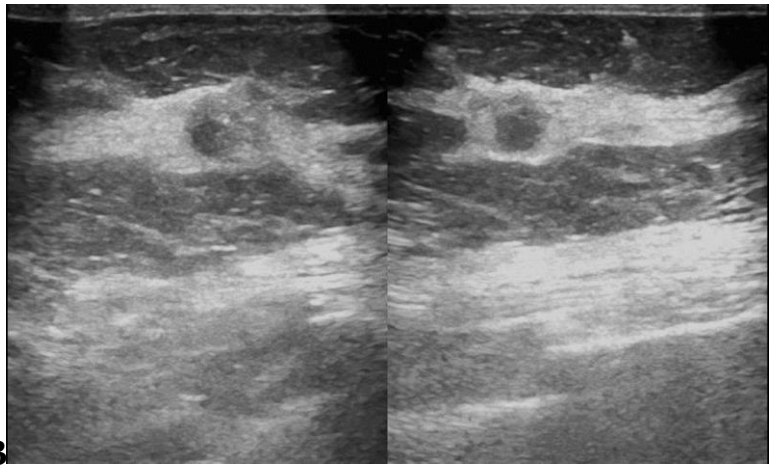
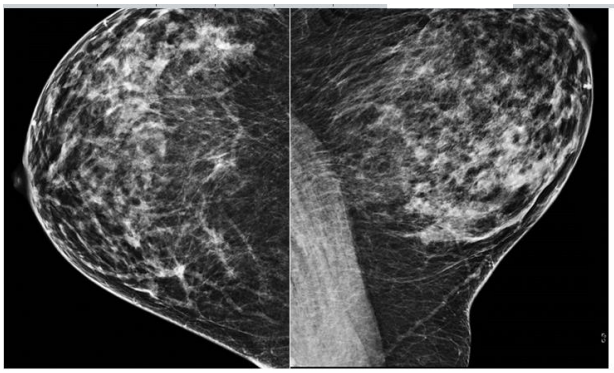


B

71 years old patient with recurrent right sided pleural effusion.(A) Right breast upper outer dense mass with marginal speculations (B) Upper outer 11 o'clock rounded hypoechoic mass with angular margin .the histopathology result show DCIS

case 2



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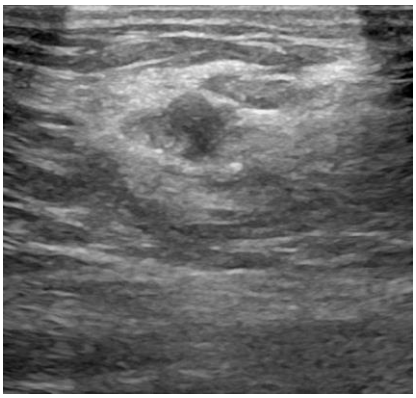

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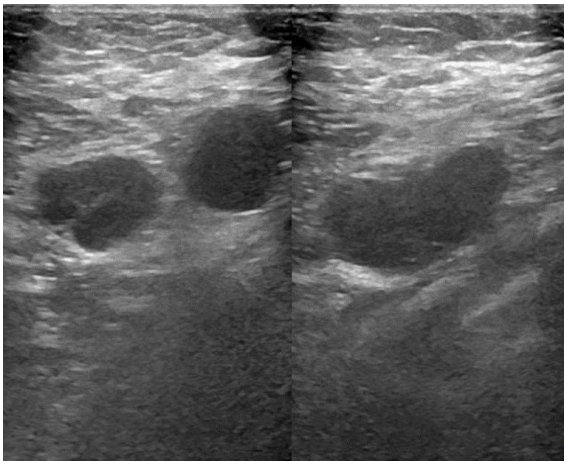
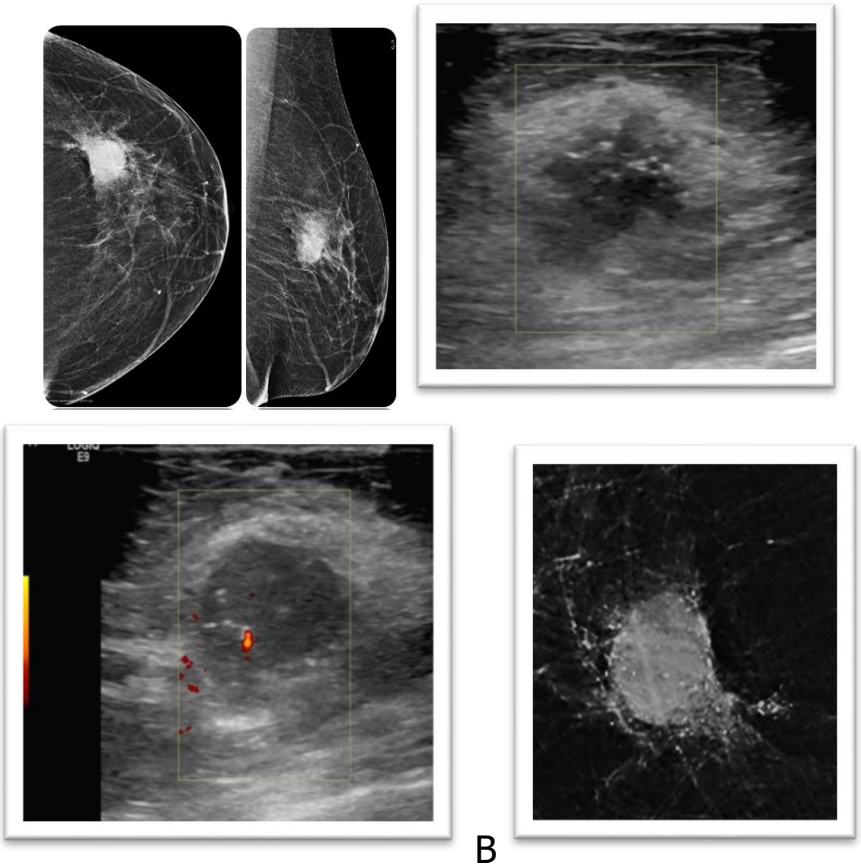


C

36 years old patient with recurrent left axillary pain. US done 1st and nothing was (A)found Left breast upper outer focal asymmetric density. Focused US on the left breast UOQ was done.(B) 3 o'clock rounded hypoechoic mass, taller than width with angular margin. Multiple Hypoechoic lymph node with lost hilum and rounded contour. Histopathology found that invasive intra ductal carcinoma

case 3

A

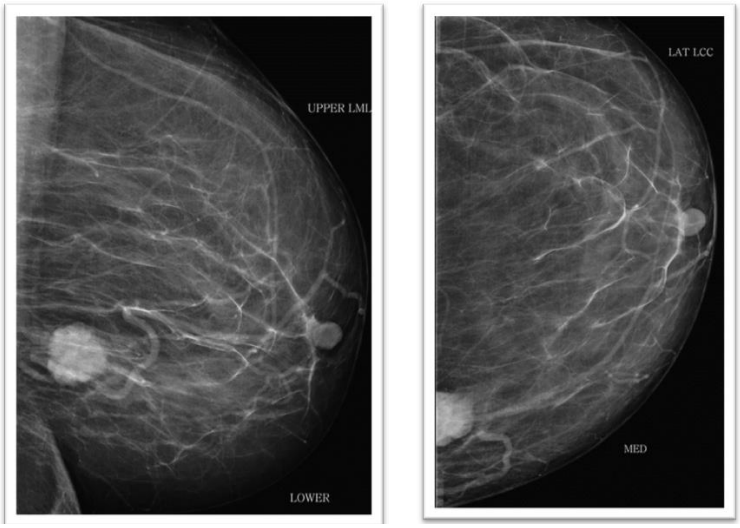


B

34 years old patient with left breast lump. Left breast upper outer partially obscured dense mass with calcifications and marginal speculations.(B) 3 o'clock speculated hypoechoic masses, taller than width with angular margin, calcifications & intralesional blood flow . histopathology result was invasive ductal carcinoma.

Case 4

A



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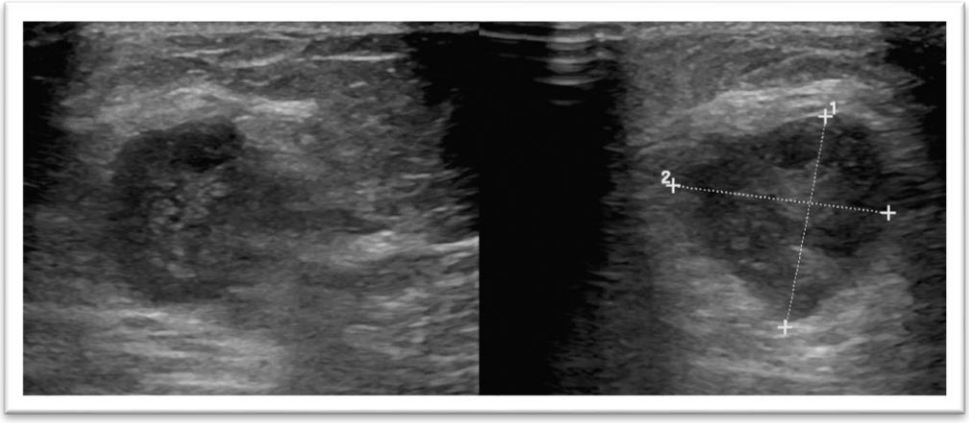
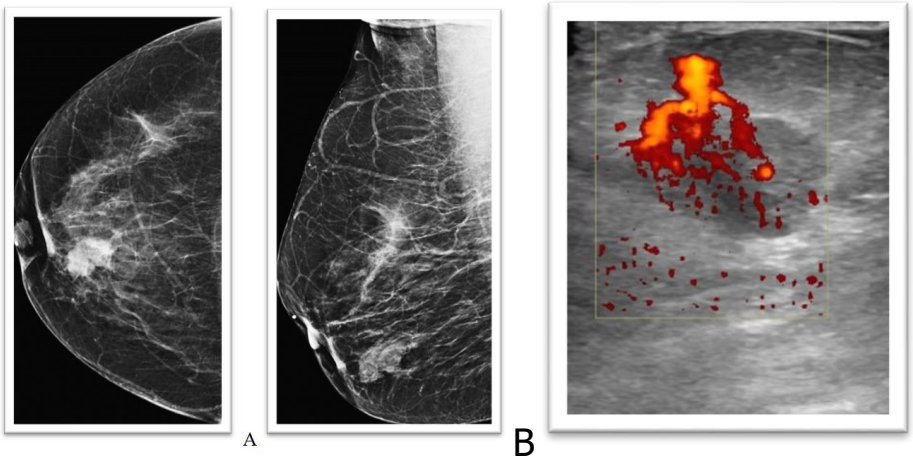
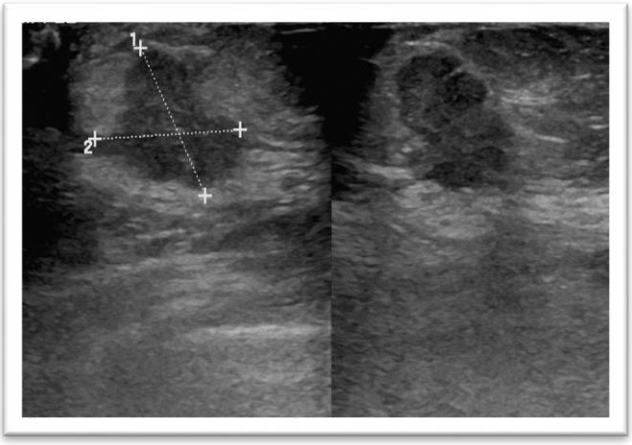


61 years old patient with left upper inner quadrant mass(A) Left breast lower inner outer dense mass with microlobulated outline.(B) 9 o'clock hypoechoic masses, taller than width with microlobulated outline. Histopathology found invasive ductal carcinoma.

Case 5



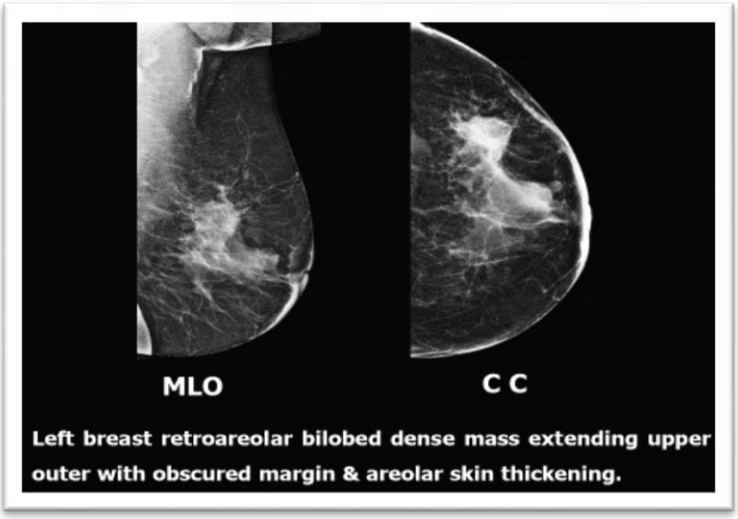
A B



C

55 years old patient with right breast lump and left breast intraductal papilloma(A) Right breast lower inner slightly dense mass with lobulated outline.(B) 4-5 o'clock hypoechoic mass, taller than width with angular margin, distal shadow & strong intralesional blood flow.

Case 6



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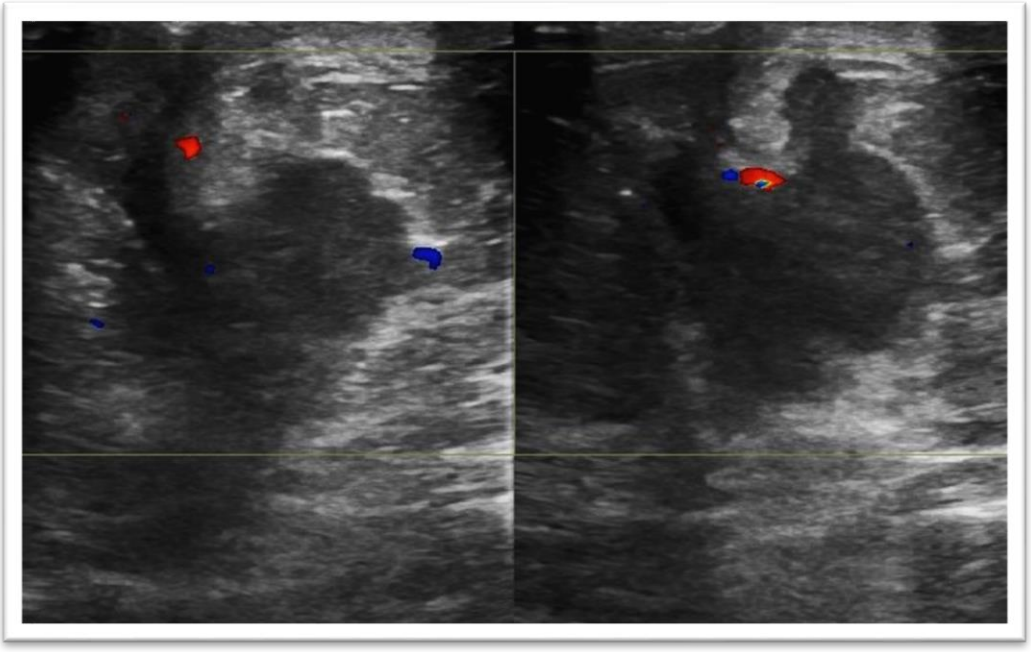
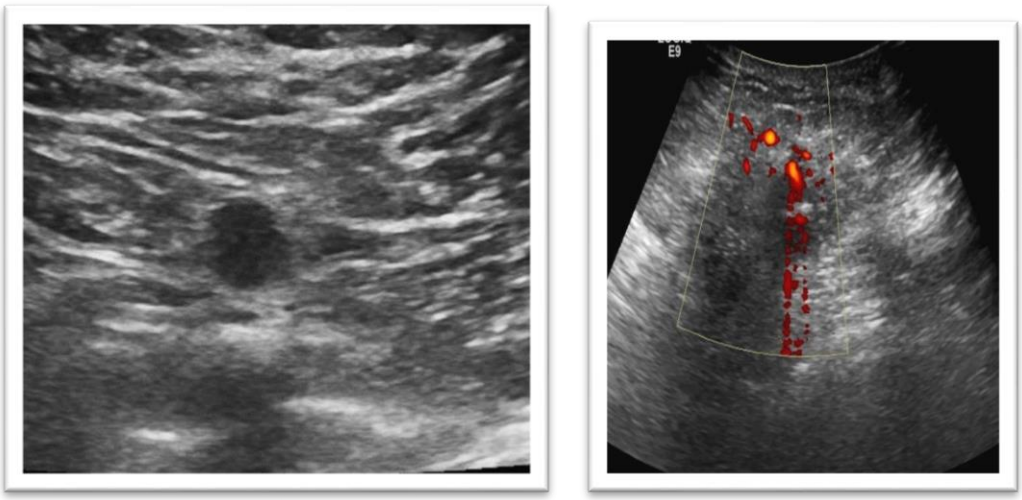


B

61 years old patient with left breast lump and nipple discharge(A) Left breast retroareolar bilobed dense mass extending upper outer with obscured margin & areolar skin thickening(B) Left breast retroareolar hypoechoic lobulated mass extending 3 o'clock outer, taller than width with angular margin, distal shadow and intralesional blood flow . histopathology result found Inflammatory carcinoma,

Case 7

A



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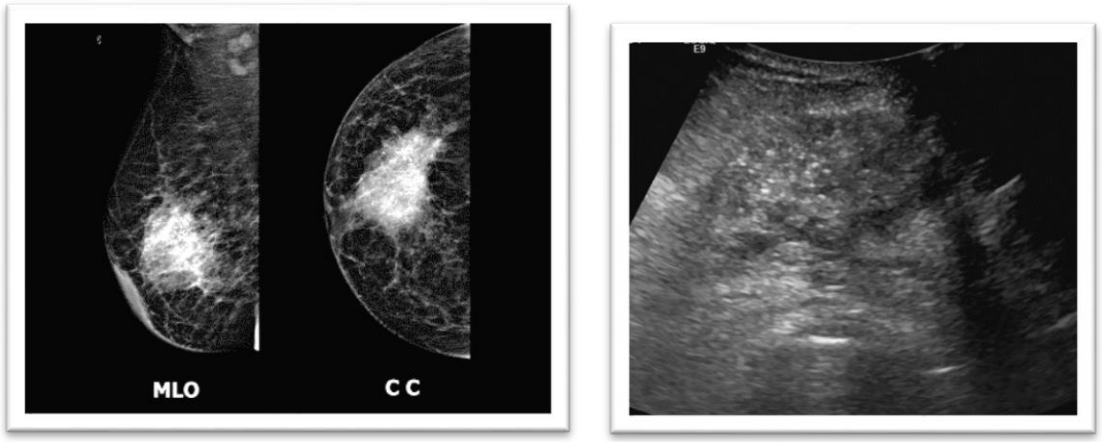
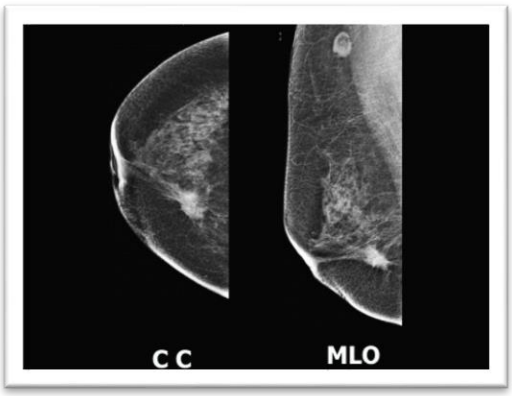


28 years old patient with right breast mass. 1st, US done.(A)9-11 o'clock large hypoechoic ares with calcifications and intralesional blood flow(B) Right breast global increased density with underlying pleomorphic calcifications and areolar skin thickening. Histopathology result invasive lobular carcinoma

Case 8



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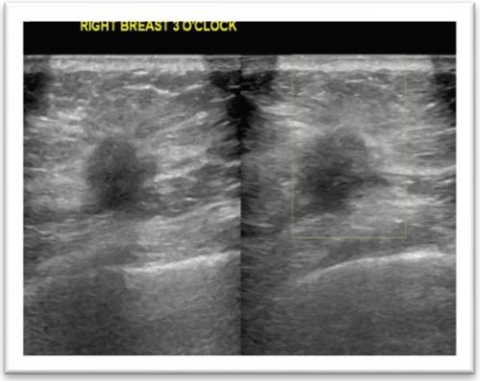

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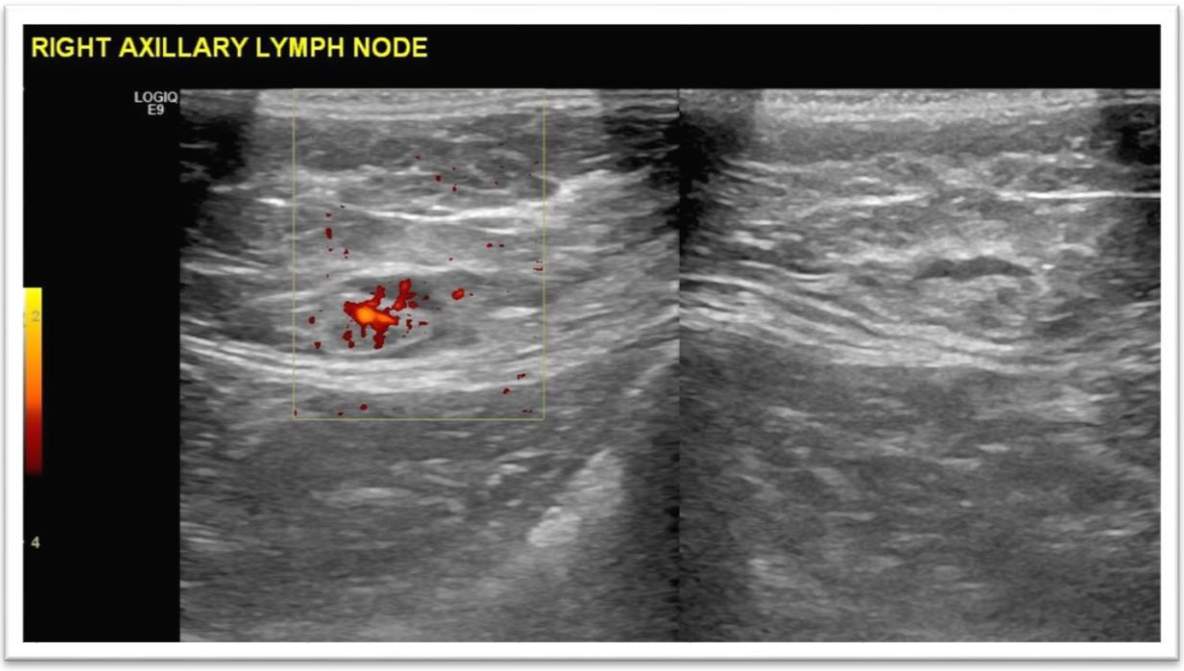


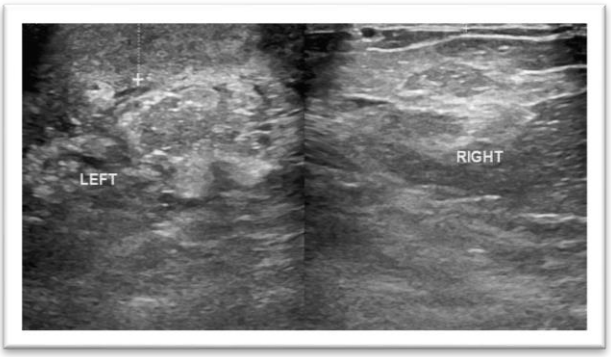
C

69 years old Right breast lump and nipple discharge.(A) Right breast lower inner speculated masses with thickened cooper ligament, nipple retraction and skin thickening and Lymph node with preserved hilum and strong peripheral vascularity (B) Right breast lower inner speculated masses with thickened cooper ligament, nipple retraction

and skin thickening. Histopathology result show the DCIS and benign lymph node

Case 9

A



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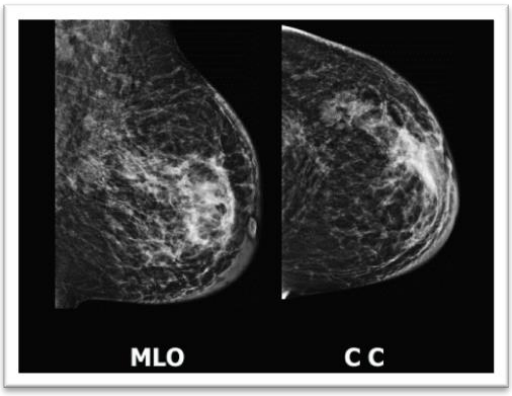

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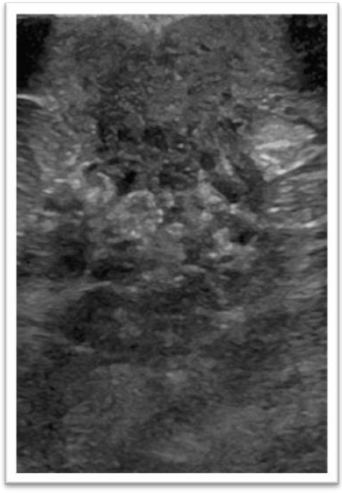
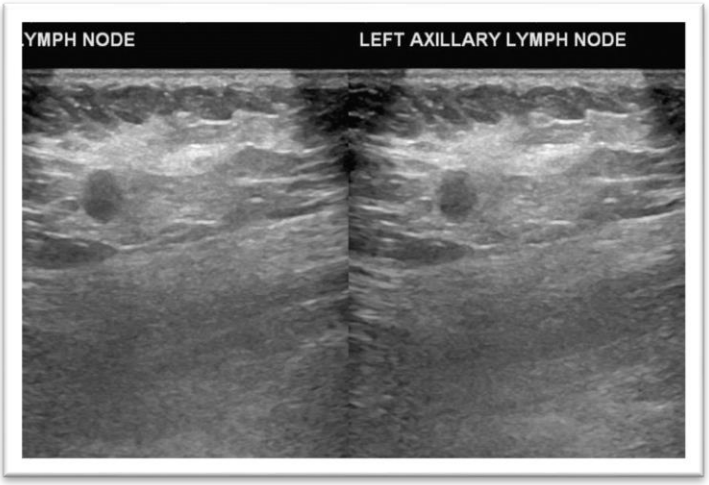


C

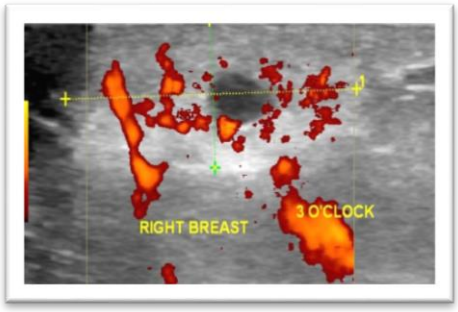


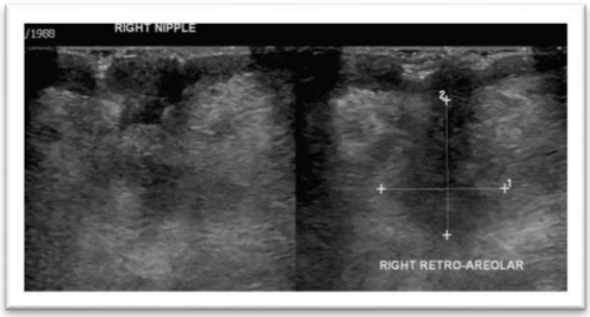
37 years old lactating patient with left breast pain, swelling and recently retracted nipple.(A) Left breast skin thickening (B) Retro areolar speculated hypoechoic mass, taller than width with and

intralesional blood flow.(C) Rounded hypoechoic lymph node with lost hilum.(D) Left breast retro areolar focal asymmetric density with nipple retraction and skin thickening . Histopatholgy result found invasive lobular carcinoma .

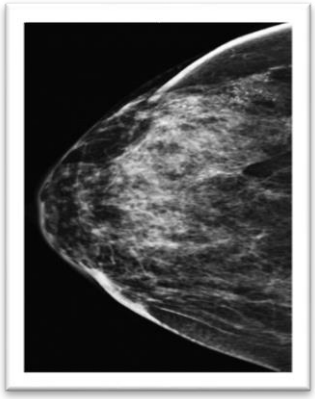
Case 10

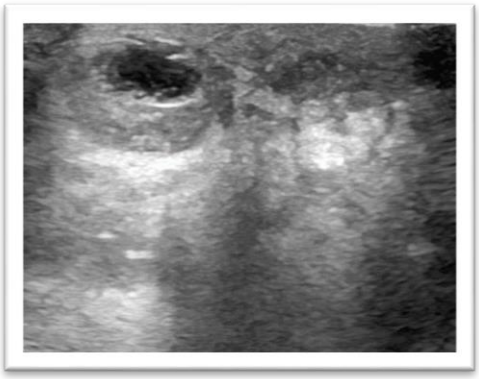
A

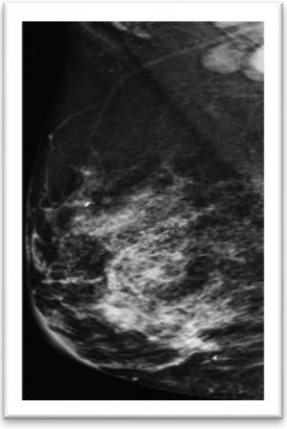




B







29 years old patient with long history of drained multiple breast abscesses.(A) Retro areolar speculated hypoechoic mass, taller than width (B) 3 o'clock complex mass with strong intralesional blood flow.(C) Right breast lateral glandular tissue focal contoural bulge with multiple grouped pleomorphic micro-calcifications in a segmental distribution and skin thickening. Histopathology result Inflammatory carcinoma.

APPENDIX(C) PUBLISHED PAPERS

- Meaad Albashir, Mohamed Yousef, Naglaa Fawzy, H.Osman, The Role of Tomosynthesis and Ultrasound Imaging In Diagnosis of Breast Lesions, Sch. J. App. Med. Sci., May 2018; 6(5): 2264-2274
- Meaad Albashir, Mohamed Yousef, Naglaa Fawzy Seleem, Awatif Omar and Amany Mamdouh Abdul Aziz, Ultrasonographic Criteria of Breast Lesions: Radiologic-Histopathologic Correlation, IJSR, Volume 7 Issue 5, May 2018