Chapter One

Introduction

1-1 Prelude:

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to investigate the anatomy and physiology of the body in both health and disease. MRI scanners use strong magnetic fields and radio waves to form images of the body. The technique is widely used in hospitals for medical diagnosis, staging of disease and for follow-up without exposure to ionizing radiation (Hollingworth W et al, 2000)

The spectrum of clinical MR examinations has hardly changed during the last decade. Brain and spine studies make up more than 50% of all studies, breast, heart and interventional studies less than 5%. FMRI (functional brain MRI) and other sophisticated examinations add up to less than 1% of all clinical MR studies (Hollingworth W et al, 2000).

Diffusion-weighted magnetic resonance imaging (DW-MRI) provides image contrast through measurement of the diffusion properties of water within tissues. Application of diffusion sensitising gradients to the MR pulse sequence allows water molecular displacement over distances of 1–20 μm to be recognised. Diffusion can be predominantly unidirectional (anisotropic) or not (isotropic). Combining images obtained with different amounts of diffusion weighting provides an apparent diffusion coefficient (ADC) map. In cancer imaging DW-MRI has been used to distinguish brain tumours from peritumoural oedema. It is also increasingly exploited to differentiate benign and malignant lesions in liver, breast and prostate where increased cellularity of malignant lesions restricts water motion in a reduced extracellular space. It is proving valuable in monitoring

treatment where changes due to cell swelling and apoptosis are measurable as changes in ADC at an earlier stage than subsequent conventional radiological response indicators. (Elizabeth M et al 2006 May).

1.2 The Problem of Study:

Biopsy is invasive method to characterize and evaluate different types of tumors with complications as invasion or bleeding may happen. MRI have different protocols to characterize the lesion

Need noninvasive accurate imaging methods for evaluating breast disease.

1.3 Objective of Study:

1.3.1 General Objective:

The purpose of this study is to evaluate the use of diffusion-weighted imaging (DWI) for the detection and characterization of breast lesions compared with dynamic contrast-enhanced MRI, dynamic curve, ultrasound, mammography and biopsy.

1.3.2 Specific Objective:

To characterize the lesion in MRI (T1, T2 and DWI for all breast lesion, To correlate the findings (DWI), sonomammoghraphy , contrast-enhanced MRI and biopsy, To find out the accuracy sensitivity and specify result of (DWI) in diagnose breast diseases, To characterize the lesion in DWI, contras enhancement and curve, To characterize the lesion ultrasound and mammography and correlate the findings with histopathology.

1.4 Significance of Study:

Diffusion weighted image (DWI) is better technique to reduce of unnecessary biopsy.

1.5 Overview of Study:

This study consisted of five chapters. Chapter one is an introduction which includes; problem and objective of the study. Chapter two is a literature review which includes; Anatomy, Physiology, Pathology and previous studies. Chapter three is about research methodology. In Chapter four the results are presented and Chapter five includes; discussion, conclusions and recommendations.

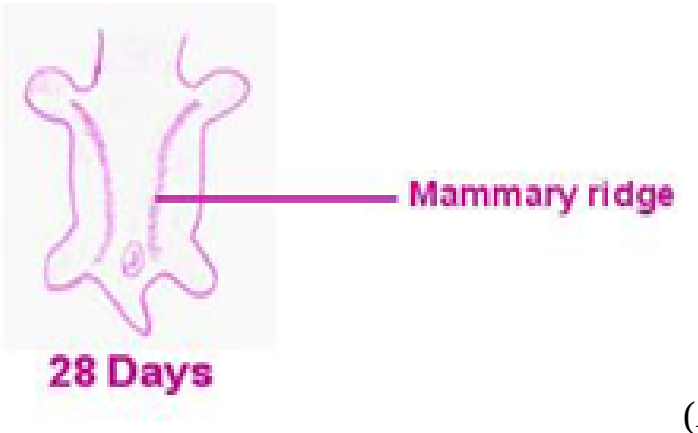
Chapter Two

Literature Review

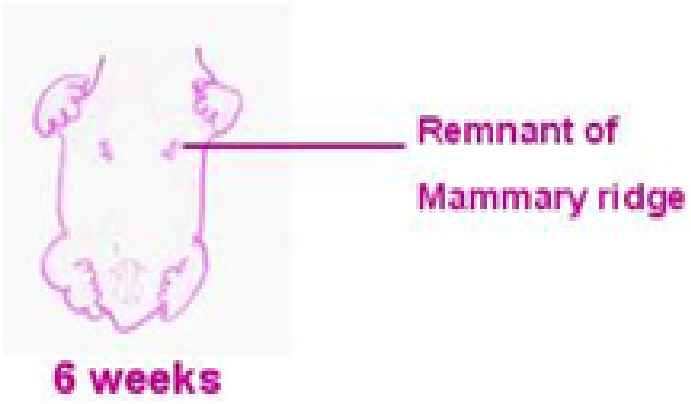
2.1 Breast Anatomy and Physiology:

2.1.1 The Embryonic Stage:

The evolution of the breast begins in the embryonic stage of gestation and continues throughout life. At the end of the third week of gestation the three primary germ layers (ectoderm, mesoderm, and endoderm) are formed. The ectoderm gives rise to the epidermis and nervous system; the mesoderm will give rise to the smooth muscle, connective tissue, blood cells and vessels, bone marrow, the bony skeleton, reproductive organs, and excretory system. The endoderm gives rise to the epithelial lining of the digestive and respiratory systems. It is also the origin of glandular cells such as hepatocytes (liver cells) and pancreatic cells, salivary glands, etc. The mammary glands are actually modified sweat glands. Their development begins along two embryological tissue lines called the milk lines. Around the twenty-eighth day of gestation mammary ridges milk ridges or milk line scan be seen on the ventral surface of the embryo. These milk lines extend bilaterally from the axilla to the groin. The embryological development of the breasts is the same in females and males. Because of their extensive coverage of embryonic breast tissue along the milk lines there can be accessory breast tissue development along its course. The mammary ridges are ectoderm tissue. Ectodermal mammary ridges should persist only in the area of the chest becoming the breasts. Breast tissue that develops anywhere along the milk lines can later manifest as abnormalities of mammary gland tissue. (Nicholas Joseph, 2006).



(A)



(B)

Figure 2-1. These two drawings (A and B) illustrate the in utero development of the human breasts. Both are ventral views, the top one at 28 days showing the mammary ridges, and again at 6 weeks showing the remains of the mammary ridges forming the breast in the chest. (Nicholas Joseph, 2006).

The mammary glands (breast) are modified sweat glands that start their embryonic development from primary buds at about the sixth week of gestation. These buds are remnants of the mammary ridges that run along the lateral ventral surfaces of the embryo. At this time the epidermis begins to involute into underlying undifferentiated mesenchymal tissue. Each primary bud develops secondary buds, which become the lactiferous ducts and its branches. Fat and connective tissues of the breast develops from mesenchymal tissue that surrounds these buds. Mammary

glands are not developed at birth, only the lactiferous ductal system. Prepubertal growth is slow although mammary ducts are in a growth phase and so is the ductal stroma. At this stage the breast consists of fat and the nipple. Then at puberty under the influence of estrogen, and to a lesser degree progestogens, corticoids, growth hormone, and prolactin the glands enlarge, fat and connective tissues proliferate. As glandular tissue and fat increase the breast enlarges giving the appearance of the female secondary sex characteristics and breast enlargement. The mammary glands are incompletely developed from puberty till pregnancy. The breast in females continues development beyond puberty becoming functionally mature just a few weeks before childbirth. In males the breast is a rudimentary organ having no normal functions at any stage of its development. (Nicholas Joseph, 2006).

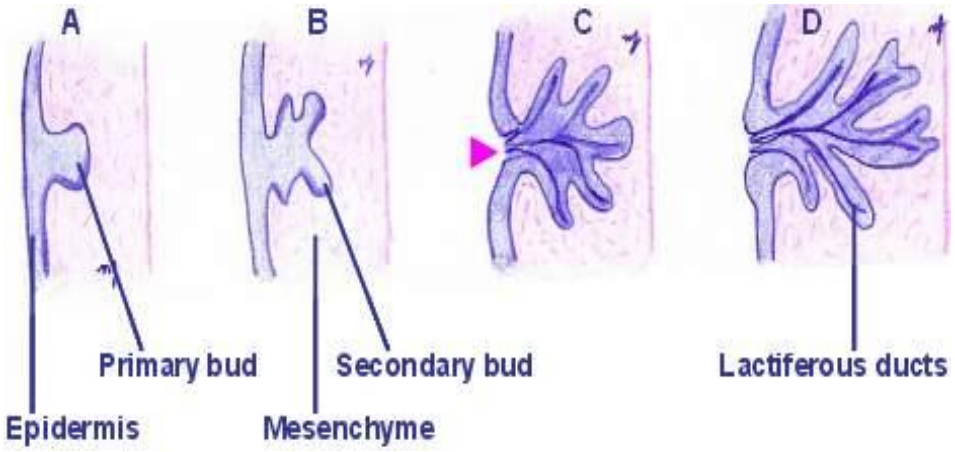


Figure 2-2. The development of the mammary glands in utero on each side of the ventral chest a primary bud (A) develops into secondary buds (B) and into lactiferous ducts and their branches (D). The lactiferous ducts are surrounded by mesenchyme that becomes connective tissue and fat. Sometime late in the fetal period (fetal period of gestation is weeks 3-9) a shallow mammary pit forms from the epidermis (pink arrow) (C). (Nicholas Joseph, 2006).

During pregnancy estrogen and progesterone levels rise and are sustained to complete the development of the mammary glands. At pregnancy the intralobular ducts of the breast undergo proliferation forming buds that become alveoli. Fat is deposited in the breast giving them an enlarged somewhat spherical (figure2-3) (Nicholas Joseph, 2006).

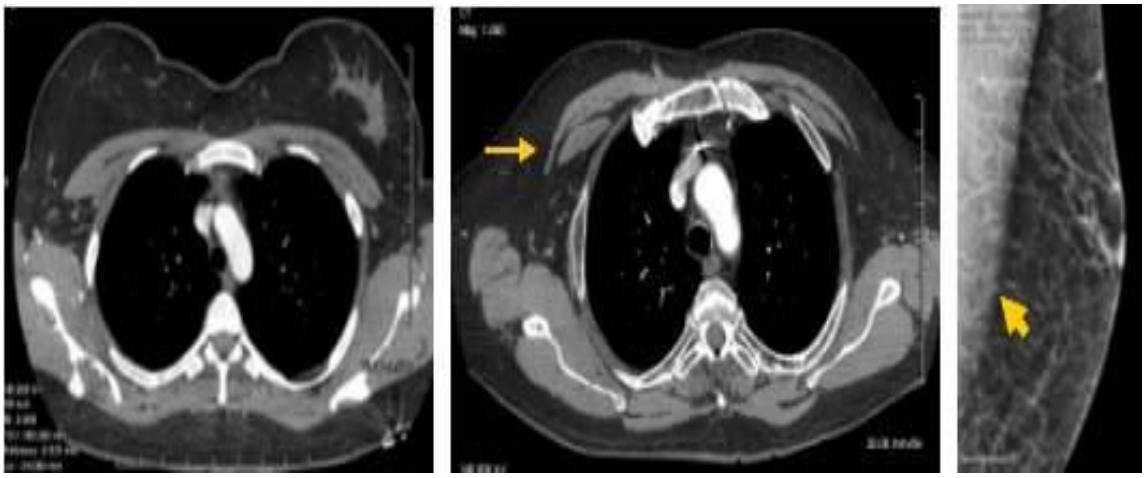


Figure 2-3. The axial CT image on the left shows the breast of an elderly woman. Notice it is mostly fatty tissue with a little glandular tissue in the left breast. (Nicholas Joseph, 2006).

The fully developed human breasts lie on the anterior chest wall atop the pectoralis major muscle. It extends from about the second rib to seventh bilaterally. The adult breast is composed of adipose, glandular and fibrous tissues. The fibrous and glandular tissues are sometimes called fibroglandular tissue. The breast is a mixture of tissues: blood vessels, secretory structures, lymphatics and fibroglandular tissue. An important anatomical space called the retromammary space lies between the pectoralis muscle and the breast. The space is filled with a layer of fat tissue. Projecting through this fat layer is a deep fascia that extends into the pectoralis muscle. It is this anatomical architecture of deep fascia invaginating into the pectoralis major that contributes to cancer metastases. Because the breast

is incompletely isolated due to continuity of deep fascia, even a radical mastectomy cannot guarantee arrest of metastases. This network of connective tissue fascia gives shape and support to the breast parenchyma. This network is commonly called the suspensory ligaments of Cooper. Cooper's ligaments and epithelial tissue traverse breast adipose tissue which surrounds the lobules and attach the breast to the anterior chest wall. There is no anatomical isolation of breast lobules to protect the breast in disease states. Advanced breast cancer near the chest wall can even penetrate into the pectoral muscles. (Nicholas Joseph, 2006).

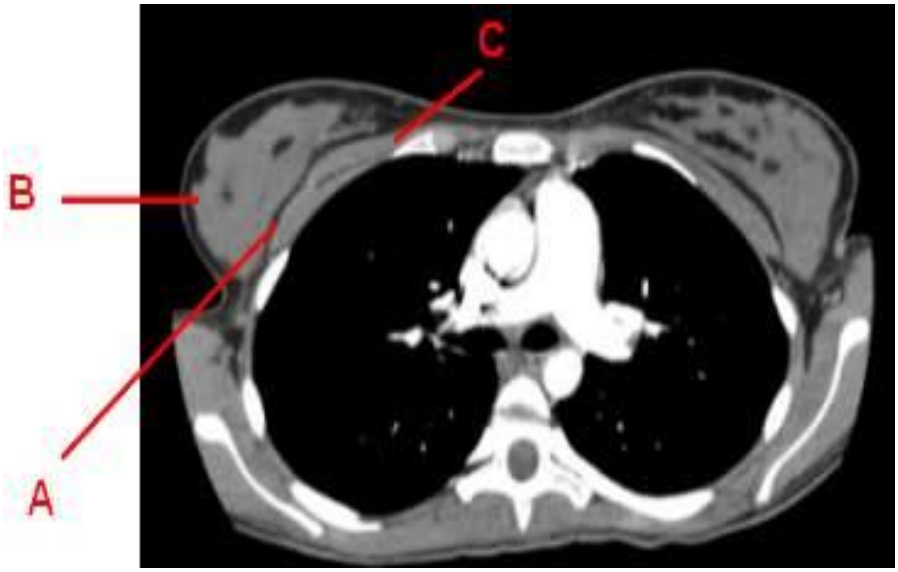


Figure 2-4.This axial CT image of a young adult female demonstrates dense fibroglandular breast tissue (B), the pectoral muscle (C), and the retromammary space (A). The breast is seen resting upon the pectoralis major muscle from which it is separated by deep fascia and fat.

2.1.2 Breast Parenchyma and Support Structures:

When we speak of the breast parenchyma we are referring to the 15-20 independent glandular lobes found in each breast. Each lobe consists of several tubulo-acinar glands arranged bulbously at different depths in the breast. Each lobe has a single lactiferous duct that drains it on the surface of the nipple (mammary papilla). At the nipple each lactiferous duct dilates slightly forming a lactiferous sinus (lactiferous ampulla). Lobes are further organized into smaller lobules each containing alveoli and an intralobular terminal duct. These are the functional units of the breast ending in a terminal unit called the terminal duct lobular unit (TDLU), and its extralobular terminal duct. The terminal duct lobular unit is the site where most lesions of the breast originate and where milk production occurs. During lactation milk is conveyed from the TDLU by way of extralobular terminal ducts to the lactiferous ducts and sinus where a small amount can be stored. About eight mammary ducts open on the surface of the nipple. . (Nicholas Joseph, 2006).

The terminal ductal lobular unit consists of the extralobular terminal ducts (ETD) and the intralobular terminal ducts (ITD). The intralobular terminal ducts are at the end of the TDLU and contain the milk-producing acinus. Each lobule can contain up to 100 terminal ductules that contain acini. The terminal duct lobular units increase and decrease with hormonal periods such as menstruation, pregnancy, lactation, oral contraception, and hormone replacement. It is important to understand that most breast cancers originate in the TDLU. When cancer is confined to the TDLU it is called in situ and when it spread out of the TDLU it becomes invasive(Figure2-5),(figure2-6) .(Nicholas Joseph,2006).

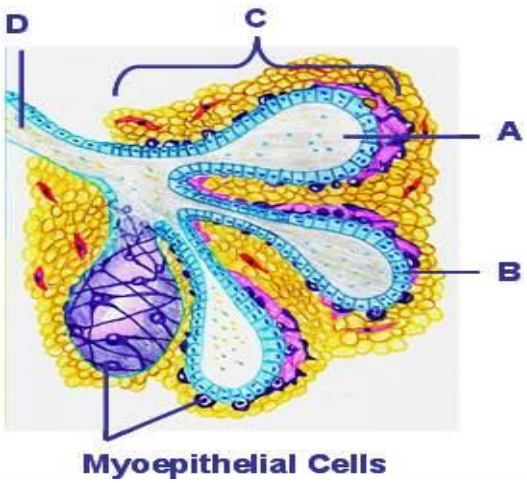


Figure 2-5. The bulbs are linked by ducts (D) surround the bulbs that squeeze. the milk producing acini (A), lining the ductile (B), and the intralobular terminal duct-ITD (C).(Nicholas Joseph,2006).

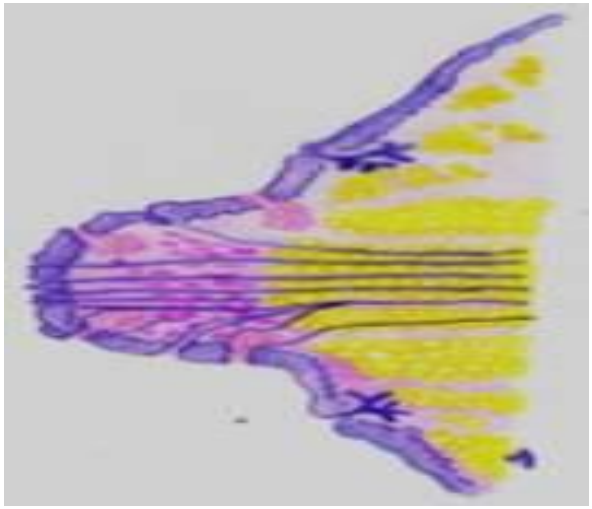


Figure2-6 .The mammary ducts along the surface of the nipple that convey milk to the nipple during lactation. . (Nicholas Joseph, 2006).

Lymphatic also drain the breast of excess intercellular fluid into the axillary region. Lymph vessels are found throughout the interlobular connective tissues and walls of the lactiferous ducts. Axillary nodes receive more than 75% of the lymph draining the gland. Most of the remainder of the lymph drains into the parasternal lymph nodes. Axillary nodes can often be seen on mammograms. They are

generally kidney bean shaped and less than 2 cm in size. Abnormal nodes on a mammogram could indicate metastasis, lymphoma, even rheumatoid arthritis, or be caused by gold injections given to treat arthritis. (Nicholas Joseph, 2006).

There are natural anatomical barriers that surround and protect the structural components of the breast. The skin, for example provides the outermost covering that protects underlying tissues from the external environment. Likewise the epidermis keeps moisture in and helps shape the breast. Deep to the skin a relatively weak capsule envelops glandular breast tissue to support the lobes and gives the breast its typical conical shape. This capsule has a natural defect in it called the foramen of Langer through which the axillary tail of Spence protrudes. Both lobes and the lobules are well encapsulated protecting the breast at all levels. The pectoral muscle and its fascia provide a posterior barrier for the breast. Loose connective tissue separates the breast from the protective fascia of the pectoral muscle; it is called the retromammary space. By far the strongest architectural barrier is the individual cell membranes of the cells of the breast parenchyma. The basement membrane lining each acinus is an important strong barrier that is not easily breached. Only aggressive cancers are able to breach the basement membrane of acini cells. A cancer that does not breach the basement membrane is called "in situ."(Nicholas Joseph, 2006).

Breast cancer most often originates in the lobules or in the ducts of the breast. Malignant disease that originates in a lobule or duct is an "in situ" cancer as long as it does not penetrate through the basement membrane. The transgression of the basement membrane is an important microscopic and biological sign that the lesion has evolved into an aggressive entity. (Nicholas Joseph, 2006).

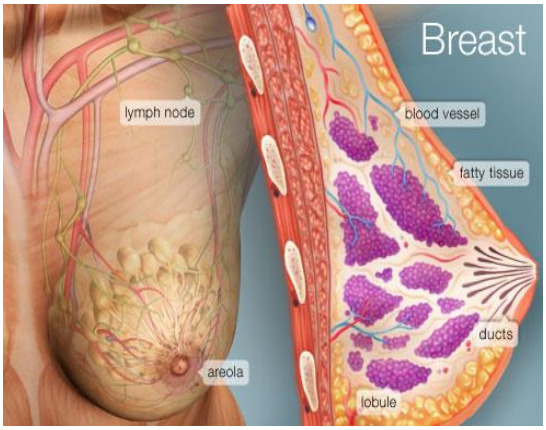


Figure2-7.Breast anatomy (WebMD, LLC.Women's Health**.** 2005-2015).

2.1.3 Vascular Anatomy and Innervation:

The blood supply to the breast skin depends on the subdermal plexus, which is in communication with deeper underlying vessels supplying the breast parenchyma. The blood supply is derived from the following:

The internal mammary perforators (most notably the second to fifth perforators), the thoracoacromial artery, the vessels to serratus anterior, the lateral thoracic artery and the terminal branches of the third to eighth intercostal perforators

The superomedial perforator supply from the internal mammary vessels is particularly robust and accounts for some 60% of the total breast blood supply. This rich blood supply allows for various reduction techniques, ensuring the viability of the skin flaps after surgery (Nicolas *G Slenkovich***,** et al 1994).

Sensory innervation of the breast is dermatomal in nature. It is mainly derived from the anterolateral and anteromedial branches of thoracic intercostal nerves T3-T5. Supraclavicular nerves from the lower fibers of the cervical plexus also provide innervation to the upper and lateral portions of the breast. Researchers believe sensation to the nipple derives largely from the lateral cutaneous branch of T4. (*Nicolas* G Slenkovich**,** et al 1994).

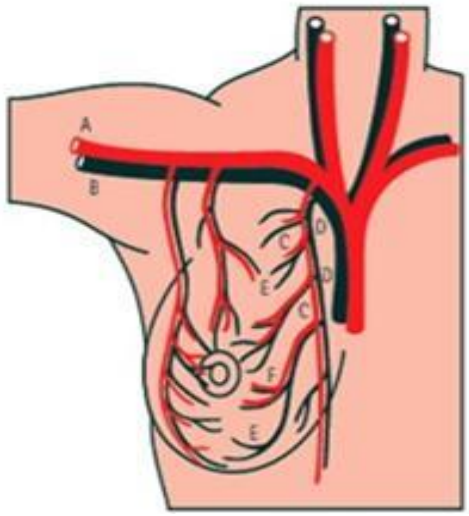


Figure2-8. Blood supply of breast (A) axillary artery, (B) axillary vien, (C) internal mammary artery, (D) internal mammary vien , (E)intercostals viens and (F)intercostal areries.(*Nicolas G Slenkovich***,** et al 1994)

2.1.4 Musculature Related to The Breast:

The breast lies over the musculature that encases the chest wall. The muscles involved include the pectoralis major, serratus anterior, external oblique, and rectus abdominis fascia. The blood supply that provides circulation to these muscles perforates through to the breast parenchyma, thus also supplying blood to the breast. They are pectoralis major, serratus anterior, rectus abdominis and External oblique (Nicolas G Slenkovich et al 1994).

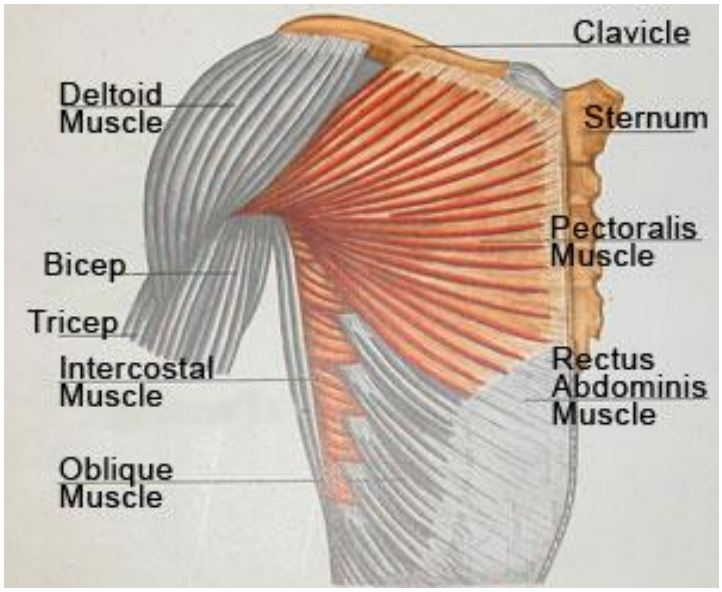


Figure2-9. Musculature Related to the Breast (Mordcai Blau, el at 2003)

2.2 Breast Shapes:

2.2.1 Common Breast Shapes:

The shape and size of a woman's breast keeps changing during her life and depends completely on genetic factors, climate conditions, diet, lifestyle and the kind of support they are given during and after development. It has been found that the shape and size of the right and left breasts for no women are identical. In fact it is quite common that one breast will be larger than the other. There are a variety of breast shapes and types. (WebMD, Med India**,** 2012).

2.2.1.1 The Perfect Breast Shape :

The Nipple is pointed outwards and is parallel to the ground. The breast should be well toned and supple with no evidence of sagging.
This breast shape is quite rare. Often when women go for cosmetic breast surgery, they are not only try to reduce or increase the size and shape of their breasts but they also wish for that perfect shape.
The perception of perfect breast shape may also vary from culture to culture. What

one society may find as the perfect breast shape, another society may brand it as not the desired shape (WebMD, Med India**,** 2012**).**

2.2.1.2 Sagging Breast:

The nipples point downwards while the breasts also droop towards the ground. Sagging of breast can be due to a variety of reasons. Usually this can be quite commonly found in women as they age towards their menopause; the Tissues holding the breast up, start to lose their elasticity and strength. (WebMD, Med India**,** 2012**).**

2.2.1.3 Swooping Breast:

The breasts do not sag but slightly bend inwards above the areola. This results in the breast to bend so the nipples point upwards and are slightly vertical to the ground. (WebMD, Med India**,** 2012**).**

2.2.1.4 Small Breast:

Are found to have very little volume of fatty tissues in them. They usually have smaller nipples and areolas with little cleavage in-between the two breasts. Hence small breasts are not always welcomed by women, Med India**,** 2012**)**.

2.2.1.5 Large Breast:

Women with large breasts have a high volume of fatty tissues in their breasts. The nipples and areolas can often be found to be bigger with women with large breasts. To prevent sagging it is vital that women with large breast wear the right kind of bra support. (WebMD, Med India**,** 2012**)**

2.2.2 Common Breast Abnormalities:

2.2.2.1 Constricted or Tubular Breast:

They are visibly narrow cylindrical or tubular in shape like egg plants. This breast shape is found to have extremely small nipples and areolas. In some cases the nipple may be overtly prominent due to the breast tissues being herniated or

squeezed into the tip. The constricted breast shape means that the two breasts are far apart due to the small base. Constricted breast shapes are classified more along the lines of being defective breast anomaly. (WebMD, Med India- Breast-Structures and types**,** 2012**).**

2.2.2.2 Pigeon or Pectus Carinatum:

These are severely deformed breasts that lie almost flat against the chest. The breastbone protrudes forward. And the breasts do not truly look like breasts. The cause of pectus carinatum is thought to be due to congenital defects. Corrective breast surgery is advised for women in this category. The surgeon usually reshapes the breasts using breast implants (WebMD, MedIndia- Breast-Structures and types**,** 2012**).**

2.2.2.3 Pectus Excavatum:

This is the opposite of the pectus carinatum. Here the chest sinks in and is also referred sometimes as the sunken chest (WebMD, MedIndia-Disease info- Breast-Structures and types, 2012)**.**

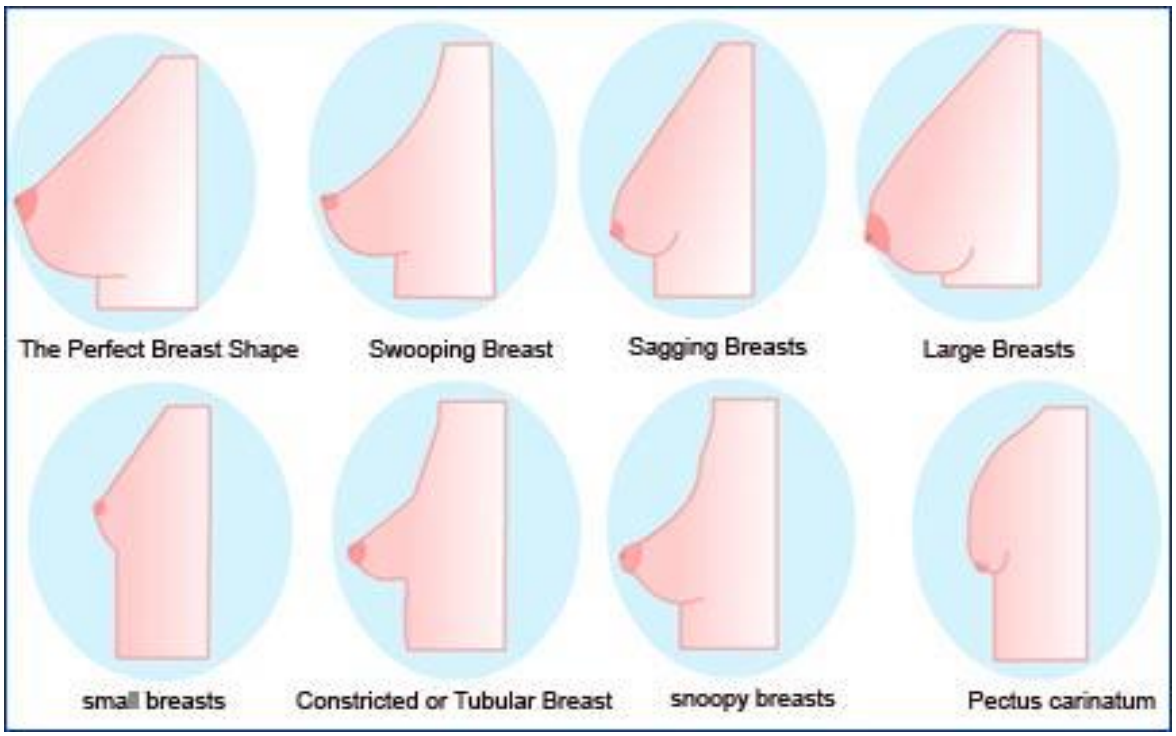


Figure2-10. Breast Shapes **(**http://www.medindia.net/patients/patientinfo/breasts-structures-and-types-breast-types.htm**)**

2.3 Pathology:

2.3.1 Benign Breast Diseases:

Benign breast conditions are very common. Women's breasts are constantly going through change, from the time of their development, through pregnancy and the menopause. This is because of the varying levels of the female hormones oestrogen and progesterone in your body.

Benign breast disease account about 80% of the breast disease. Very few benign disease have an ability to become malignant.

Many breast changes will be diagnosed as being a benign breast condition that may or may not need treatment. (http://www.breastcancer.org)

2.3.1.1 Breast Pain:

Breast pain is very common in women of all ages. Approximately two out of three pre-menopausal women (women who haven't been through the menopause) will experience it at some time in their lives. There are two main categories of breast pain cyclical breast pain and non-cyclical breast pain(http://www.breastcancer.org)

2.3.1.2 Breast Calcification:

Breast calcifications are small spots of calcium salts. They can occur anywhere in the breast tissue. They are very small, so you won't be able to feel them, and they don't cause any pain.

Breast calcifications are mostly benign .However, sometimes calcifications can be an early sign of breast cancer.

Breast calcifications are very common and usually develop naturally as the breast tissue ages. Sometimes they form because of other changes in the breast, such as a fibroadenoma or breast cyst. (http://www.breastcancer.org)

2.3.1.3 Breast Cysts:

They are one of the most common causes of a breast lump, and can develop in either one or both breasts. It's thought that they develop naturally as the breast changes with age, due to normal changes in hormone levels. It's common to have more than one cyst.

Sometimes, fluid-filled sacs develop in the breast tissue; these are breast cysts.

Breast cysts development at any age, they are most common in women over 35 who haven't yet reached the menopause. They develop more often as women get closer to the menopause and usually stop once a woman has been through the menopause. However, women who are take hormone replacement therapy (HRT) after the menopause may also develop cysts. (http://www.breastcancer.org)

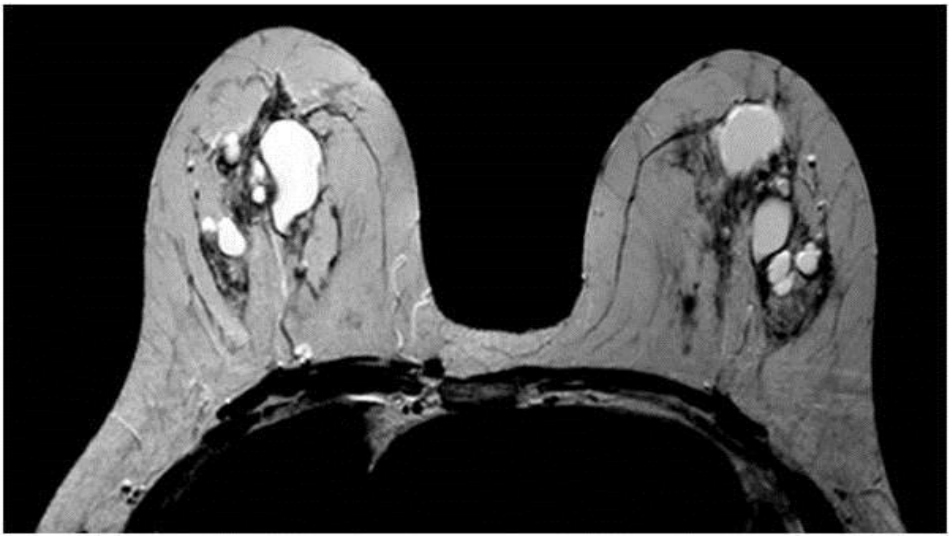


Figure2-11.T2 WI shows multiple bilateral simple cysts.

(http://dx.doi.org/10.1594/ecr2012/C-1385)

2.3.1.4 Duct Ectasia:

As women reach the menopause and the breasts age, the ducts behind the nipple get shorter and wider (this is called ectasia). This is a normal breast change and nothing to worry about.

Sometimes a secretion can collect in the widened ducts and their lining can become irritated. The lining can also become ulcerated and painful as well, although this is not common. This is a benign (not cancer) condition called duct ectasia.

Duct ectasia can also cause a discharge from the nipple, which is usually thick but may also be watery. The discharge can vary in colour and can be either clear or bloodstained. (http://www.breastcancer.org)

2.3.1.5 Fat Necrosis:

Sometimes a lump can form if an area of the fatty breast tissue is damaged. This is called fat necrosis.

Fat necrosis feels like a firm, round lump and is usually painless, but in some people it may feel tender or even painful.

Sometimes within an area of fat necrosis cysts containing an oily fluid can occur. These are called oil cysts. (http://www.breastcancer.org).

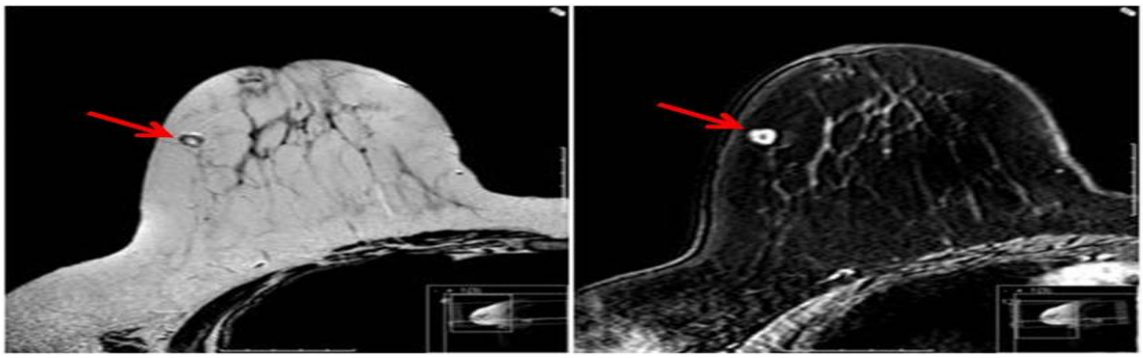


Figure 2-12 .T2WI and Contrast enhanced T1WI with fat necrosis (http://dx.doi.org/10.1594/ecr2012/C-1385)

2.3.1.6 Fibroadenoma:

Fibroadenomas develop from a lobule. It is don't increase the risk of developing breast cancer. They are thought to occur because of an increased sensitivity to the female hormone oestrogen.

A fibroadenoma usually has a smooth rubbery texture and can move easily under the skin. Fibroadenomas are usually painless, but some people may feel some tenderness or even pain.

Fibroadenomas are very common and it is not unusual to have more than one. They are mostly found in young women, but can occur at any age.

Most fibroadenomas are about 1 to 3cm in size and are called simple fibroadenomas. There are Hyperplasia, and atypical hyperplasia (http://www.breastcancer.org)

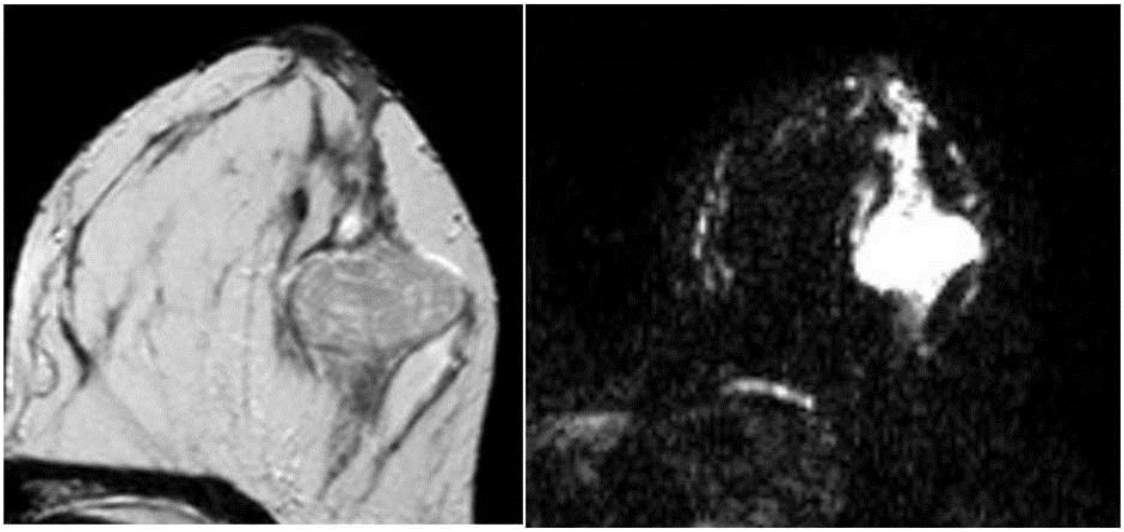


Figure2- 13. T2 WI and DWI show a Myxoid Fibroadenoma

(http://dx.doi.org/10.1594/ecr2012/C-1385)

2.3.1.7 Intraductal Papilloma:

Sometimes a wart-like lump develops in one or more of the ducts. It's usually close to the nipple, but can sometimes be found elsewhere in the breast. Patient feel a small lump or notice a discharge of clear or bloodstained fluid from the nipple. Generally intraductal papillomas aren't painful but some women can experience pain around the area. All of these may be symptoms of an intraductal papilloma (http://www.breastcancer.org)

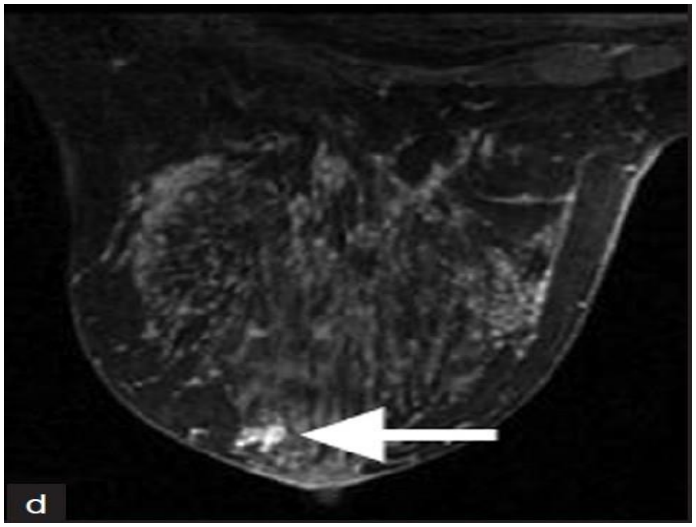


Figure 2-14.Intraductal Papilloma (http://dx.doi.org/10.1594/ecr2012/C-1385)

2.3.1.8 Lobular Neoplasia:

When lobular neoplasia occurs, there is an increase in the number of cells contained in the lobules, together with a change in their appearance and behaviour. The term 'lobular neoplasia' describes a range of changes within the breast lobules including atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). In situ means the changes only occur in the breast lobules and do not affect the surrounding tissue. (http://www.breastcancer.org)

2.3.1.9 Periductal Mastitis:

Periductal mastitis occurs when the ducts under the nipple become inflamed and infected. It's a benign condition, which can affect women of all ages but is more common in younger women. (http://www.breastcancer.org).

2.3.2 Malignant Breast Diseases:

Classifications of breast cancer are ductal carcinoma and lobular carcinoma.
The most common type of breast cancer is ductal carcinoma occurring in slightly over 90% of all cases. Lobular carcinoma affects another 5-10% of women. (http://www.breastcancer.org).

2.3.2.1 Ductal Carcinoma in Situ (DCIS):

It's the most common type of non-invasive breast cancer. Ductal means that the cancer starts inside the milk ducts. Carcinoma refers to any cancer that begins in the skin or other tissues (including breast tissue) that cover or line the internal organs, and in situ means "in its original place.
DCIS is called "non-invasive" because it hasn't spread beyond the milk duct into any normal surrounding breast tissue. DCIS isn't life-threatening, but having DCIS can increase the risk of developing an invasive breast cancer later on. (http://www.breastcancer.org.)

2.3.2.2 Invasive Ductal Carcinoma(IDC):

Sometimes called infiltrating ductal carcinoma, is the most common type of breast cancer. About 80% of all breast cancers are invasive ductal carcinomas.
Invasive means that the cancer has "invaded" or spread to the surrounding breast tissues. (IDC) refers to cancer that has broken through the wall of the milk duct and begun to invade the tissues of the breast. Over time, it can spread to the lymph nodes and possibly to other areas of the body. Invasive ductal carcinoma can affect women at any age, it is more common as women grow older. It is also affects men. (http://www.breastcancer.org).

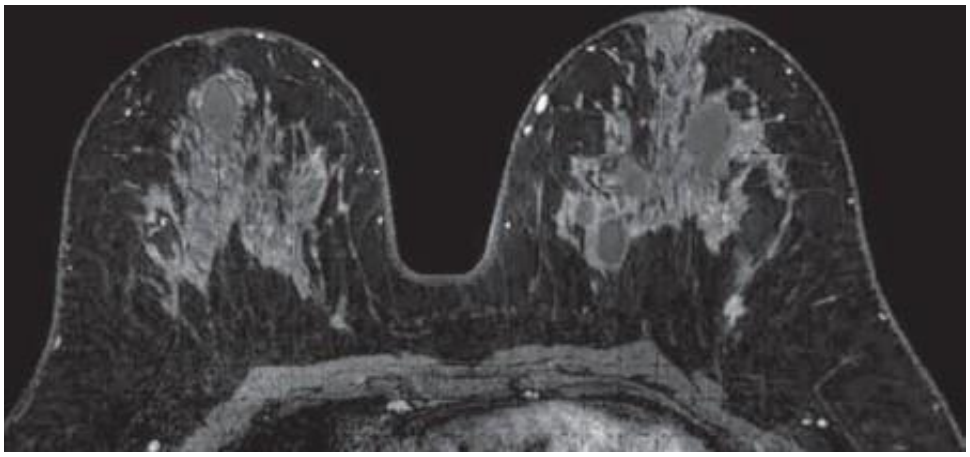


Figure2- 15. Invasive Ductal Carcinoma IDC (http://www.auntminnie.com)

2.3.2.3 Invasive Ductal Carcinoma (IDC) Types:

First Tubular Carcinoma of the breast: is usually small (about 1 cm or less) and made up of tube-shaped structures called "tubules." tubular carcinomas accounted for about 1-4% of all breast cancers.

Second Medullary Carcinoma of the breast: is accounting for about 3-5% of all cases of breast cancer. It is called “medullary” carcinoma because the tumor is a soft, fleshy mass that resembles a part of the brain called the medulla. It usually affects women in their late 40s and early 50s.

Third Mucinous Carcinoma of the breast: sometimes called colloid carcinoma — is a rare form of (IDC). The tumor is made up of abnormal cells that “float” in pools of mucin. Mucinous carcinoma is less likely to spread to the lymph nodes than other types of breast cancer, about 2-3% of invasive breast cancers are “pure” mucinous carcinomas it tends to affect women after they’ve gone through menopause.

Forth Invasive papillary carcinomas of the breast are rare, accounting for less than 1-2% of (IDC). In most cases, these types of tumors are diagnosed in older women who have already been through menopause. An invasive papillary carcinoma usually has a well-defined border and is made up of small, finger-like projections.

In most cases of invasive papillary carcinoma, ductal carcinoma in situ (DCIS) is also present.

Fifth in Invasive Cribriform Carcinoma: the cancer cells invade the stroma in nest like formations between the ducts and lobules. It is usually low grade, meaning that its cells look and behave somewhat like normal, healthy breast cells. In about 5-6% of invasive breast cancers, some portion of the tumor can be considered cribriform. Usually, some ductal carcinoma in situ (DCIS) of the cribriform type is present as well. (http://www.breastcancer.org).

2.3.2.4 Lobular Carcinoma in Situ (LCIS):

It's the abnormal cells start growing in the lobules, the milk-producing glands at the end of breast ducts. Lobular means that the abnormal cells start growing in the lobules, the milk-producing glands at the end of breast ducts. Carcinoma refers to any cancer that begins in the skin or other tissues that cover internal organs — such as breast tissue. In situ or “in its original place” means that the abnormal growth remains inside the lobule and does not spread to surrounding tissues. People diagnosed with LCIS tend to have more than one lobule affected. LCIS is usually diagnosed before menopause, most often between the ages of 40 and 50. Less than 10% of women diagnosed with LCIS have already gone through menopause. (http://www.breastcancer.org).

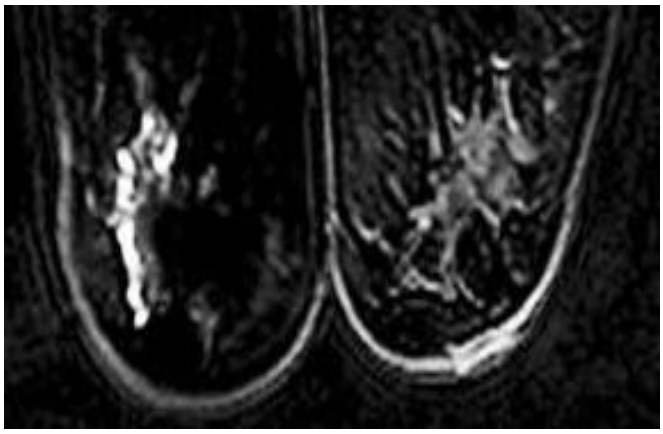


Figure2-16. Lobular Carcinoma in Situ LCIS in contras enhancement in MRI (http://breast-cancer.ca/mag-lex)

2.3.2.5 Invasive Lobular Carcinoma (ILC):

Sometimes called infiltrating lobular carcinoma is the second most common type of breast cancer after (IDC). Invasive means that the cancer has “invaded” or spread to the surrounding breast tissues. Lobular means that the cancer began in the milk-producing lobules, which empty out into the ducts that carry milk to the nipple. About 10% of all invasive breast cancers are invasive lobular carcinomas. (About 80% are invasive ductal carcinomas.) It is more common as women grow older. About two-thirds of women are 55 or older when they are diagnosed with an invasive breast cancer. ILC tends to occur later in life than invasive ductal carcinoma the early 60s as opposed to the mid to late 50s (http://www.breastcancer.org)

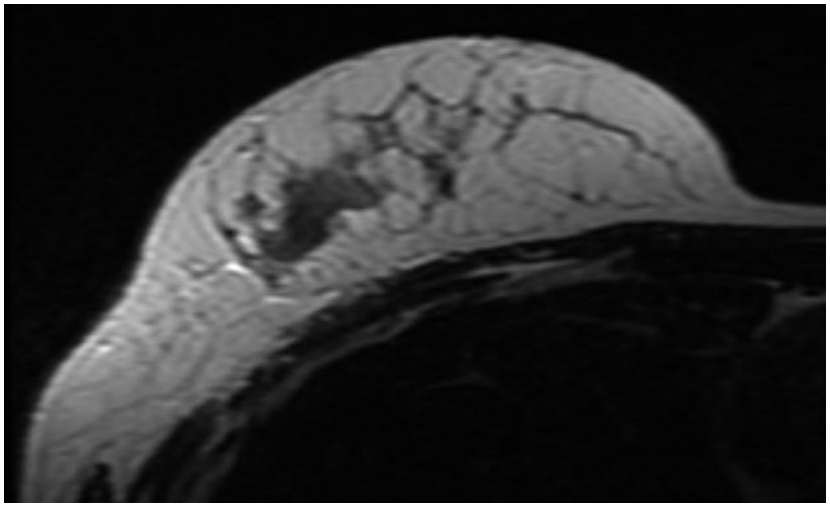


Figure 2-17. Invasive Lobular Carcinoma ILC in T2
(http://radiopaedia.org/articles/invasive-lobular-carcinoma-of-the-breast

2.3.2.6 Inflammatory Breast Cancer (IBC):

It's a rare and aggressive form of breast cancer. Inflammatory breast cancer usually starts with the reddening and swelling of the breast instead of a distinct lump. IBC tends to grow and spread quickly, with symptoms worsening within days or even hours. It’s important to recognize symptoms and seek prompt treatment. (http://www.breastcancer.org).

2.4 Breast Cancer Risk Factors:

2.4.1 Established Risk:

Being a woman is the biggest risk factor for developing breast cancer, about two out of three invasive breast cancers are found in women 55 or older, first-degree female relative (sister, mother, and daughter) diagnosed with breast cancer, your risk is doubled, about 5% to 10% of breast cancers are thought to be hereditary, personal history of breast cancer 3 to 4 times more likely to develop a new cancer, radiation therapy to the chest or face before age 30, race/Ethnicity, white women are slightly more likely to develop breast cancer than African American, Hispanic, and Asian women, overweight and obese women have a higher risk especially after menopause, women who haven't had a full-term pregnancy or have their first child after age 30, breastfeeding history, especially if a woman breastfeeds for longer than 1 year, started menstruating younger than age 12 or lasts beyond age 55, use postmenopausal hormone replacement therapy (HRT), a drinking alcohol, use of oral contraceptives, Having dense breasts can be 6 times more likely to develop cancer, Lack Exercise lower risk of breast cancer, and smoking causes a higher risk of breast cancer in younger, premenopausal women. (http://www.breastcancer.org)(Nicholas Joseph, 2006).

2.4.2 Emerging Risks:

Low of Vitamin D Levels, Light Exposure at Night that women who work at night -- factory workers, doctors, nurses, and police officers, DES (Diethylstilbestrol) Exposure, Eating Unhealthy Food responsible for about 30% to 40% of all cancers, Exposure to Chemicals in Cosmetics, Exposure to Chemicals in Food, Exposure to Chemicals for Lawns and Gardens, Exposure to Chemicals in Plastic, Exposure to Chemicals in Sunscreen, Exposure to Chemicals in Water, and Exposure to Chemicals When Food Is Grilled/Prepared. (http://www.breastcancer.org) (Nicholas Joseph, 2006).

2.5 Breast Cancer Stages:

2.5.1 Stage Usually Expressed as a Number on a Scale of 0 Through IV:

Stage 0:
Stage 0 is used to describe non-invasive breast cancers

Stage I:

Stage I describes invasive breast cancer.

Stage I is divided into subcategories known as IA and IB.

Stage II:

Stage invasive breast cancer. Stage II is divided into subcategories known as IIA and IIB.

Stage III:

Stage invasive breast cancer. Stage III is divided into subcategories known as IIIA, IIIB, and IIIC.

Stage IV:

Stage IV describes invasive breast cancer that has spread beyond the breast and nearby lymph nodes to other organs of the body, “metastatic”
(http://www.breastcancer.org)

2.5.2 Certain Words Used to Describe The Stage of The Breast Cancer:

Local: The cancer is confined within the breast.

Regional: The lymph nodes, primarily those in the armpit, are involved.

Distant: The cancer is found in other parts of the body as well. (http://www.breastcancer.org

(table2-1): breast cancer survival rates by stage (Nicholas Joseph,2006).

Breast Cancer Survival Rates by Stage		
Stage		**5-year Survival Rate**
0	Carcinoma in situ	100%
I	Tumor < 1 cm, negative axillary nodes	98%
IIA	Tumor 2-5 cm, negative or positive nodes	88%
IIB	Tumor > 5 cm, negative nodes	76%
IIIA	Tumor > 5 cm, positive nodes	56%
IIIB	Any size tumor, spread to breast skin, internal breast lymph nodes, or to the chest wall	49%
IV	Any size tumor, distant metastasis	16%

2.5.3 TNM classification system:

TNM (Tumor, Node, and Metastasis) is another staging system researchers use to provide more details about how the cancer looks and behaves. The doctors might mention the TNM classification, but less then use the numerical staging system. Sometimes clinical trials require TNM information from participants.

The TNM system is based on three characteristics:

Size (T stands for tumor), lymph node involvement (N stands for node), whether the cancer has metastasized (M stands for metastasis), or moved beyond the breast to other parts of the body.

The T (size) category describes the original (primary) tumor:

TX means the tumor can't be measured or found.

T0 means there isn't any evidence of the primary tumor.

T is means the cancer is "in situ" (the tumor has not started growing into healthy breast tissue).

T1, T2, T3, and T4: These numbers are based on the size of the tumor and the extent to which it has grown into neighboring breast tissue. The higher the T number, the larger the tumor and/or the more it may have grown into the breast tissue.

The N (lymph node involvement) category describes whether or not the cancer has reached nearby lymph nodes:

NX means the nearby lymph nodes can't be measured or found.

N0 means nearby lymph nodes do not contain cancer.

N1, N2, and N3: These numbers are based on the number of lymph nodes involved and how much cancer is found in them. The higher the N number, the greater the extent of the lymph node involvement.

The M (metastasis) category tells whether or not there is evidence that the cancer has traveled to other parts of the body:

MX means metastasis can't be measured or found.

M0 means there is no distant metastasis.

M1 means that distant metastasis is present.

For example, a T1 N0 M0 breast cancer would mean that the primary breast tumor is less than 2 centimeters across (T1), has not involved the lymph nodes (N0), and has not spread to distant parts of the body(M0).This cancer would be grouped as stage I (http://www.breastcancer.org).

2.6 Methods of Breast Investigation:

2.6.1 Breast Zones:

For the purpose of describing areas of the breast self-examination (BSE) and mammography imaging each breast is conventionally divided into four quadrants and the axillary tail. But before we describe these zones it is pertinent to discuss the importance of monthly breast self-exam (BSE). (Nicholas Joseph, 2006).

2.6.2 Four Quadrants:

The upper outer quadrant (UOQ), upper inner quadrant (UIQ), lower outer quadrant (LOQ), and lower inner quadrant (LIQ). Each quadrant is further subdivided using the clock face model. The 12 o'clock position is above the nipple and the 6 o'clock position below the nipple. Care must be used when describing the location of a lesion in the right vs. the left breast since the 2 o'clock position in the left breast would be in the UOQ, but the 2 o'clock position in the right breast would be in the UIQ. (Nicholas Joseph, 2006).

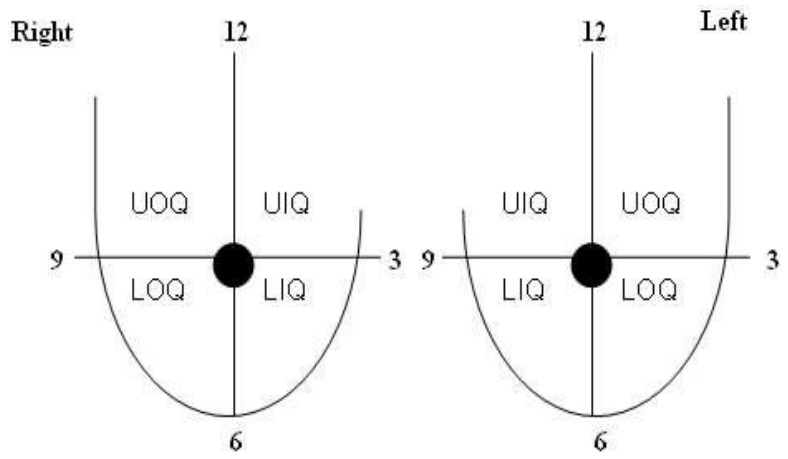


Figure 2-18. Four quadrants:

(Nicholas Joseph, 2006).

2.6.3 Breast-Self Examination(BSE):

Patient stand: with hands alongside examine breasts for change in size or shape or texture of the skin. This is a visual examination of each breast. Then raise your arms above a head and re-examine the size and shape of each breast (Nicholas Joseph, 2006).

Lying Down: Examine each breast, for example, to examine the left breast put a pillow under left shoulder. Then raise left arm above y a head and rest arm. Using a right hand, examine the left breast in the following manner: use the pads of a middle fingers to go over the breast in either a circular motion, up and down motion, or a wedge motion (moving fingers in and out towards the nipple). Keep a fingers on the breast until the entire breast is examined including the underarm area. Repeat procedure on the right breast. (Nicholas Joseph, 2006).

When Showering: Perform the exam upright just as she would when lying down. It can be easier to slide the hand along the breast when the skin is wet and soapy. The important thing to remember is that she should either use the lying down or shower method routinely. (Nicholas Joseph, 2006).

In addition to the breast self-examination, women over 40 should have an annual clinical breast examination (CBE) (Nicholas Joseph, 2006).

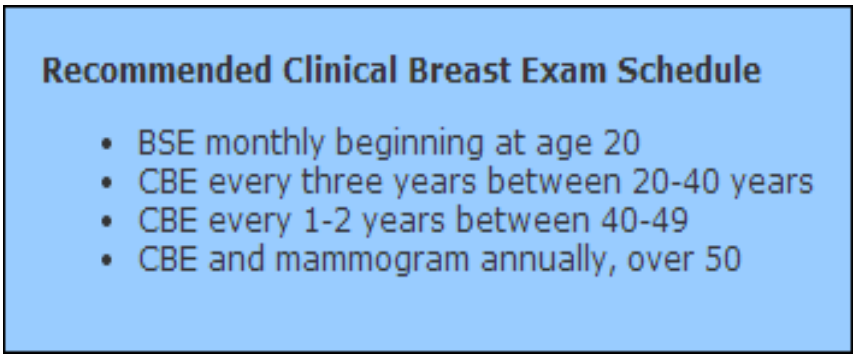


Figure2-19. Clinical breast examination (Nicholas Joseph, 2006).

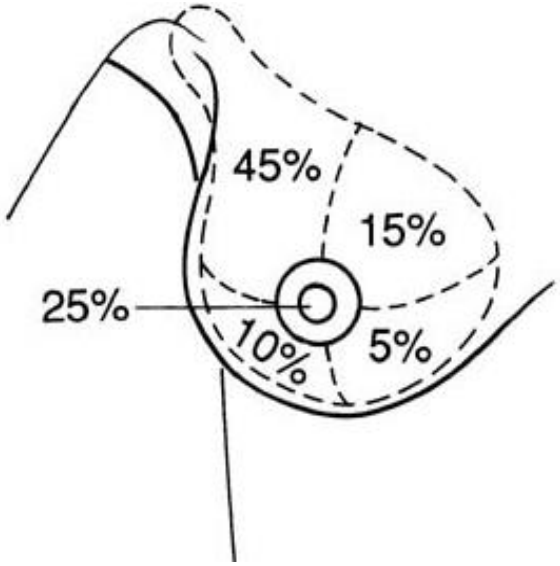
If a lump is found, note size, consistency and whether is attached to skin or underlying tissue (http://www.Improving outcomes in breast cancer -NICE Clinical Guideline, 2002).

Table2-2. The features of palpable breast masses (http://www.Improving outcomes in breast cancer -NICE Clinical Guideline, 2002).

Clinical features of palpable breast masses	
Malignant breast masses	Benign breast masses
Consistency: hard	Consistency: firm or rubbery
Painless (90%)	Often painful (consistent with benign breast conditions)
Irregular margins	Regular or smooth margins
Fixation to skin or chest wall	Mobile and not fixed
Skin dimpling may occur	Skin dimpling unlikely
Discharge: bloody, unilateral	Discharge: no blood and bilateral discharge. Green or yellow colour
Nipple retraction may be present	No nipple retraction

2.7 The Distribution of Cancers by Region:

Posterior to the nipple – 25%; upper outer quadrant – 45%; upper inner quadrant – 15%; lower outer quadrant – 10%; lower inner quadrant – 5%. When performing the breast self-exam the patient should be taught to examine the upper outer quadrant and axillary tail, and the area posterior to the nipple very well since this is where most cancers are found. (Fiugre2-20). ((http://www.bImproving outcomes in breast cancer -NICE Clinical Guideline, 2002).



Fiugre2-20. Clinical quadrants of the breast with the percentage of all cancers of the breast found in each. (http://www.Improving outcomes in breast cancer -NICE Clinical Guideline, 2002).

2.8 Image of Breast:

2.8.1 Ultrasound of Breast:

Ultrasound imaging involves exposing part of the body to high-frequency sound 15 -10 MHz waves to produce pictures of the inside of the body. An ultrasound scan does not use ionizing radiation (x-ray).

Imaging Specialists offers the most advanced technology in ultrasound scans. Ultrasound imaging adds the additional dimension of motion. Because ultrasound images are captured in real-time, they can show the structure and movement of the body's internal organs, as well as blood flowing through blood vessels.

The advantages of advanced ultrasound include:

Real time, high resolution images, increased image penetration, greater detailed visualization and reduced exam times. (http://www.imaging specialties, 2014)

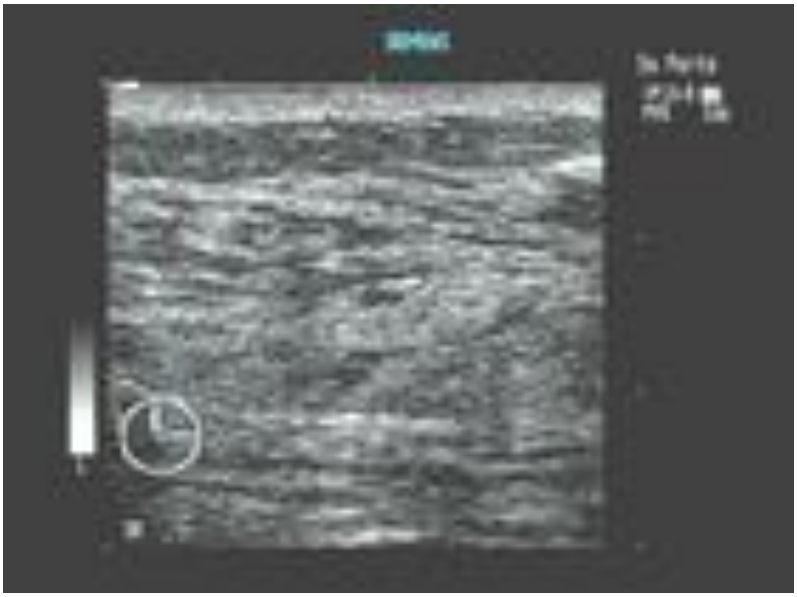


Figure2-21. Normal ultrasound breast

http://www.imaginis.com/mammography/ultrasound-images-of-breast-conditions-1

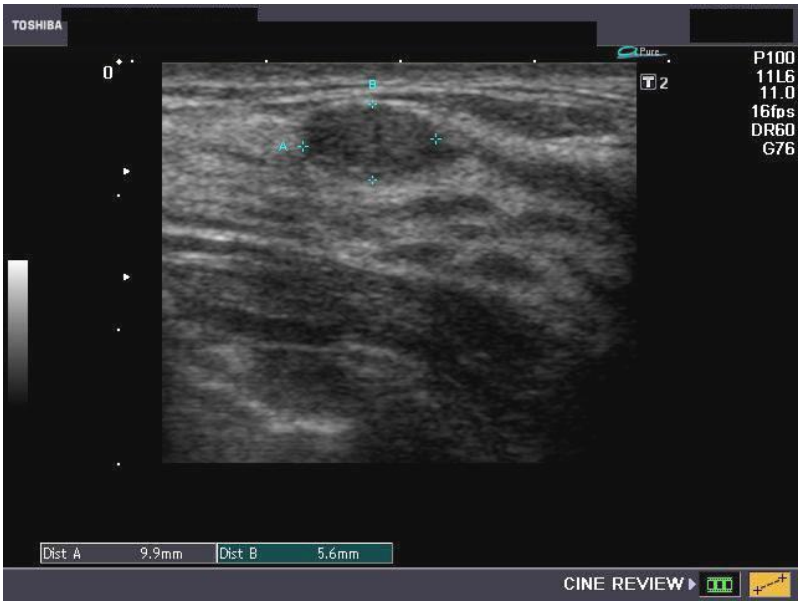


Figure 2-22.Breast fibroademoa Ultrasound image (http://www.ultrasound-images.com/breast.htm#Fibroadenoma of breast)

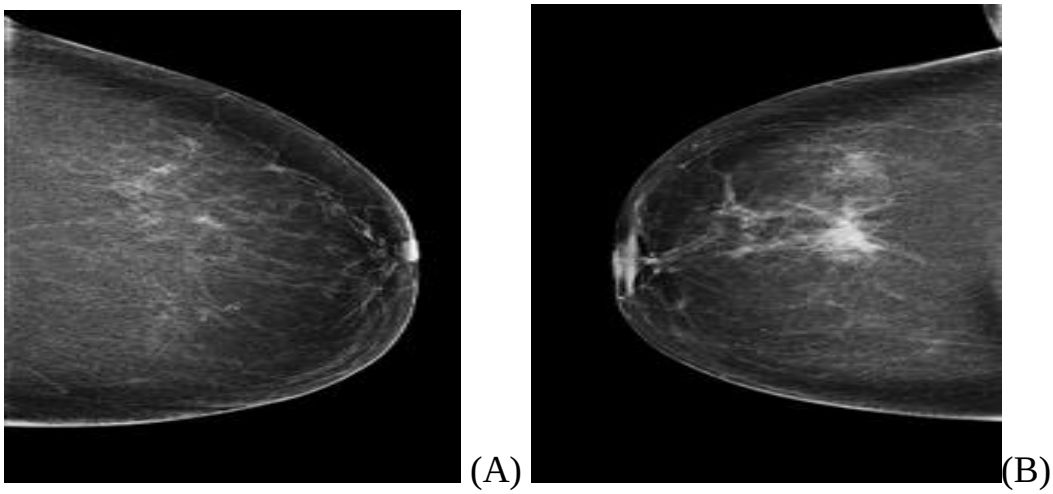
2.8.2 Mammography:

Digital mammography is a specific type of imaging that uses a low-dose x-ray system to examine breasts. A mammography exam, called a mammogram, is used to aid in the diagnosis of breast diseases in women.

Mammography plays a central part in early detection of breast cancers because it can show changes in the breast up to two years before a patient or physician can feel them. Research has shown that annual mammograms lead to early detection of breast cancers, when they are most curable. (http://www.imaging specialties, 2014)

Mammography positions:

Mediolateral Oblique View (MLO), Cranio-Caudal View (CC), Medio-Lateral View (ML) and Latero-Medial View (LM).



(A) (B)

Figuer2-23.Mammogram images (A) left normal breast and (B) right breast with lesion.

(http://www.diagnijmegen.nl/index.php/Earlier_detection_of_breast_cancer_by_computer_assisted_decision_making_in_screening)

2.8.3 MRI Breast:

2.8.3.1 Image planes:

Bilateral sagittal imaging of the breast can lead to decrease of signal-to-noise ratio SNR and spatial resolution. Therefore, current bilateral imaging protocols use the transverse or coronal plane. Coronal imaging of the breast tends to give more respiratory motion artifacts. Also, nipple and chest wall involvement is more difficult to detect on coronal images. Therefore, the transverse imaging plane is preferred when bilateral breast imaging is performed (Kuhl, 2007).

2.8.3.2 Spatial and temporal resolution:

Breast MRI needs to be performed with adequate spatial resolution in order to assess lesion morphology accurately. It is widely adopted that an optimal breast MRI should have a minimum size threshold for detection of lesions of 5 mm. Therefore, a voxel size of at least 2.5 mm in any direction should be used. However, higher in-plane spatial resolution results in more accurate lesion morphology assessment. Therefore, the minimal in-plane spatial resolution as recommended by the American College of Radiology is < 1 mm (Weinstein et al., 2010).

2.8.3.3 DWI characteristics:

the apparent diffusion coefficient (ADC), which characterizes the mobility of water molecules in vivo and indirectly reflects tissue cellularity, microstructural characteristics and membrane integrity (Le Bihan D et al 1992).

2.8.3.4 Focal, mass-, and nonmass-like enhancement:

Focal enhancement can be described as small (less than 5 mm) area of enhancement that cannot be specified otherwise. A mass is a lesion that is visible in three dimensions and which occupies a space. Masses can be round, oval, lobulated, or irregular, and may have smooth, irregular, or spiculated margins. Nonmass-like enhancement is an area of enhancement that does not belong to a three dimensional mass or that has no distinct mass characteristics (Erguvan-Dogan et al., 2006), it has a 32% chance of being malignant.

Nonmass-like enhancement patterns can be divided in linear, ductal, segmental, and regional enhancement

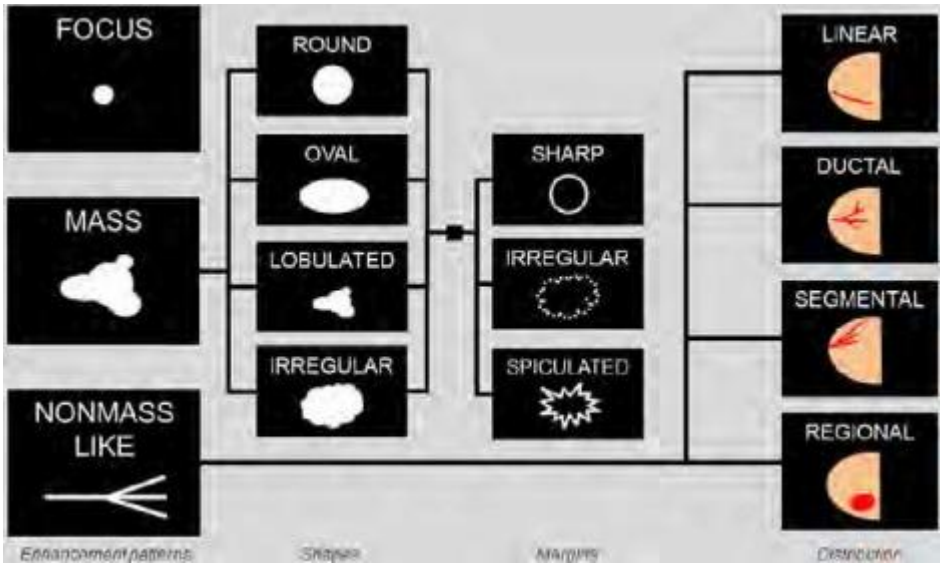


Figure2-24.Proper terminology (according to the BI-RADS lexicon) for enhancement patterns, shapes, margins, and nonmass-like enhancement distributions. (Erguvan-Dogan et al, 2006).

Linear nonmass-like enhancement in a line that is not definitely in a duct'. Ductal enhancement can be defined as 'enhancement in a line that points towards the nipple, and may have branching, conforming to a duct'. Segmental enhancement can be defined as 'a triangular region or cone of enhancement, with the apex pointing towards the nipple.

Finally, regional enhancement can be defined as 'enhancement in a large volume of tissue not conforming to a ductal distribution (Erguvan-Dogan et al., 2006).

2.8.3.5 Morphologic descriptors:

2.8.3.5.1 Morphologic descriptors in masslike- and nonmass-like enhancement:

Margins of masses can be described as smooth (or sharp), irregular, or spiculated. Similar to mammography, some morphologic features of a lesion are more associated with malignancy than others (Liberman et al., 1998). The spiculated margins, irregular shapes, and linear/ductal nonmass-like enhancement had the highest positive predictive values for malignancy (Nunes et al., 1997, 2001).it has an 80% chance of being malignant.

2.8.3.5.2 Morphologic descriptors inT1-T2 characteristics:

High signal on T1

the pre-contrast T1, non-fat-suppressed sequence can show the presence of fat in a lesion.

Central high signal on a T1-weighted image can be seen in intramammary lymph nodes or fat necrosis.

Fat is also seen in hamartomas.Breast lesions containing fat are benign unless they are rapidly growing.

Rapidly growing lesions should be biopsied (Leong Cs et al, 2000).

High signal on T2-fatsat:

In T2 fat-suppressed images we are looking for water. Lesions that are bright on T2 include cysts, lymph nodes and fat necrosis.

These are all benign lesions.

Unfortunately there is one malignant lesion that has a high signal intensity on T2 fat-suppressed weighted images. This is the colloid carcinoma.

It is the exception to the rule that all things with bright signal on T2 fat-suppressed images are benign (Leong Cs et al, 2000).

Moderate and low signal on T2-fatsat:

The T2 fat-suppressed sequences are for detecting lesions with high signal, not moderate or low signal.

Moderate and low signal intensities can be caused by cancer (table 2-3) (Leong Cs et al, 2000).

Table2-3.compare between moderate and low signalhttp://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html

2.9 Diffusion-Weight Magnetic Resonance Imaging:

2.9.1 Introduction:

The excellent soft tissue contrast of magnetic resonance imaging (MRI) has made it an invaluable technique in oncological assessment. A variety of pulse sequences providing a range of contrast allows detailed evaluation of the size and spread of disease and, to some extent, the heterogeneity within a tumour or its metastases—i.e. the presence of cysts or necrosis or the existence of a vascularized rim. The majority of clinical MR measures the rate at which signal from hydrogen nuclei (protons) in a static magnetic field decays following perturbation by a sequence of pulses. This decay is described by the protons' T1 and T2 relaxation rate. Mobile protons, such as those present in a small water molecule, take a relatively long time for their signal to decay in the detector plane and, as a result, the long T2 values produce a large signal on T2-weighted imaging. Protons attached to larger, less mobile fatty molecules have smaller T2 values, that is, their signal decays quickly and results in a lower signal intensity on a T2-weighted image. Pathological processes within tissue such as edema, necrosis or fibrosis change the water content and vascularity of tissue, and hemorrhage affects local magnetic fields, leading to susceptibility effects. Thus, the presence of a tumour causes changes in the tissue that may alter its T1 or T2 relaxation rates, and be manifest as observable changes on conventional T1- and T2-weighted images. However, changes in T1 and T2 relaxation are often insufficient to detect or characterize the lesion. (Mori S, Barker et al PB.1999).

Another mechanism for developing image contrast is through 'apparent diffusivity' (the displacement of tissue water due to random, thermally driven motion over distances of ~1–20μm). The visualization of changes in the diffusion properties of tissue water with MR imaging has become a useful, multifaceted tool to

characterize tissue structure and to identify and differentiate disease processes The degree of motion measured by DW-MRI relates to the mean path length 'L' travelled by protons in the body within a specific observation time period (its 'diffusion time') as a result of thermally driven, random motion. Mori S, Barker et al PB.1999).

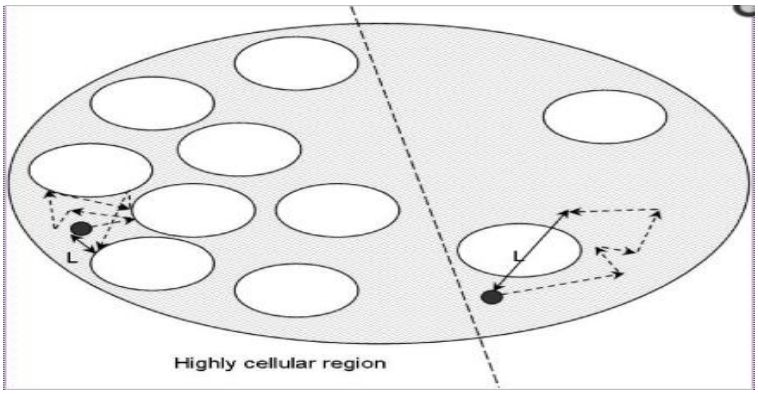


Figure2-25. A representation of a tumour or tissue displaying heterogeneous cellularity (Mori S, Barker et al PB.1999).

2.9.2 Technique:

2.9.2.1 Imaging Sequences:

Also demonstrates that signal loss is proportional to the motion component in the same direction as the diffusion gradient. No signal loss would occur if the motion was perpendicular to the gradient direction. DW-MRI is thus sensitive not only to the extent to which protons are free to diffuse but also to their preferential diffusion direction. Both magnitude and direction of diffusion are influenced by the architecture of the tissue under investigation. (Rowley HA el at 1999).

2.9.2.2 Technical Limitations:

DW-MRI can be adversely affected by artifact from motion other than diffusion. As molecular displacement of the order of micrometres is being observed on diffusion-weighted images, it is no surprise that any motion, even vascular pulsation, interferes with these measurements. Motion present within the body, e.g. voluntary, respiratory, even arteriole level perfusion is capable of producing displacement much greater than that to which DW-MRI has been sensitized. The need to develop 'snap-shot' imaging techniques, to account for bulk motion, has been achieved largely via the implementation of echo-planar imaging (EPI). Single-shot EPI can acquire a complete image within a second, single-shot, or in multiple shots employing navigator MR signals for each shot to correct for bulk motion. While single-shot methods are robust to motion, their elevated sensitivity to magnetic field inhomogeneities leads to image distortion and artifacts in areas exhibiting large variations in magnetic susceptibility, e.g. air–tissue interfaces, or chemical-shift effect, e.g. fat–water interfaces. Owing to the effects of chemical shift, single-shot EPI is performed with fat suppression as standard, the quality of the fat suppression being of great importance in extracranial applications. Spatial resolution tends to be sacrificed to obtain high imaging speeds and signal averaging is likely to be necessary to increase signal-to-noise ratio (SNR), especially when using larger values of diffusion sensitive gradients. A train of single-shot EPI images acquired with a long TR are T2- or $T2^{*}$-weighted, their effective TE being the time at which the central lines of k-space are filled. Strong frequency encoding gradients enable images to be acquired with a shorter effective TE and consequently better SNR. Multi-shot methods can provide better spatial resolution with fewer image distortion artifacts and higher SNR, but are not as

robust to the effects of motion and require acquisition times of 10 min or more. (Rowley HA,el at .1999).

2.9.2.3 Image Analysis:

A DW-MRI sequence's sensitivity to diffusion (characterised by its b-value) can be adjusted by altering the combination of gradient pulse amplitude, the time for which the gradients are applied and the time that elapses between their application (sometimes termed 'diffusion time'). The higher the b-value, the more sensitive an image is to the effects of diffusion. (Rowley HA,el at .1999)

Lower b-values (50–100 s/mm^2) suppress the signal in highly mobile water molecules, resulting in signal loss of vessels. "Black-blood" images have less diffusion weighting but higher SNR and less distortion artifacts.

High b-values (500–1000 s/mm^2) only tissues with high cellular density such as tumor, neurologic, or lymphatic tissue show a high signal. (Rowley HA,el at .1999) The maximum b-value should be adapted to the typical ADC of the corresponding tissue. Thus, b-values for abdominal imaging are usually lower than for neuroimaging.

Signal loss in DW-MRI is proportional to the component of molecular displacement in the same direction as that of the diffusion gradient (Rowley HA, Grant PE, and Roberts TP. Diffusion MR imaging: theory and applications. Neuroimaging (Clin N Am, 1999). In some areas of the body, such as in the brain, tissue architecture such as fiber tracts makes it much easier for tissue water to diffuse in a specific direction, e.g. water diffuses preferentially along rather than perpendicular to myelinated axons. This property is exploited in MR tractography where diffusion tensor imaging (DTI) can create a tensor for each image voxel which describes diffusion in multiple directions. (Le Bihan D, el at 2001).

At least six independent diffusion-encoding directions are required for such a technique. Alternatively, for some applications, it may be desirable to 'average out' the effects of preferential directions of diffusion. Most clinical machines now offer the capability to create ADC maps by averaging three diffusion-weighted images which have encoded diffusion in the slice, frequency (read) and phase-encode directions respectively. Such techniques are termed 'isotropic' and the associated averaged ADC maps sometimes termed 'trace' or 'isotropic'. (Le Bihan D, et al 2001).

Signal loss in DW-MRI is proportional to the component of molecular displacement in the same direction as that of the diffusion gradient. In some areas of the body, such as in the brain, tissue architecture such as fibre tracts makes it much easier for tissue water to diffuse in a specific direction. Preferentially along rather than perpendicular to myelinated axons. This property is exploited in MR tractography where diffusion tensor imaging (DTI) can create a tensor for each image voxel which describes diffusion in multiple directions. (Le Bihan D et al, 2001).

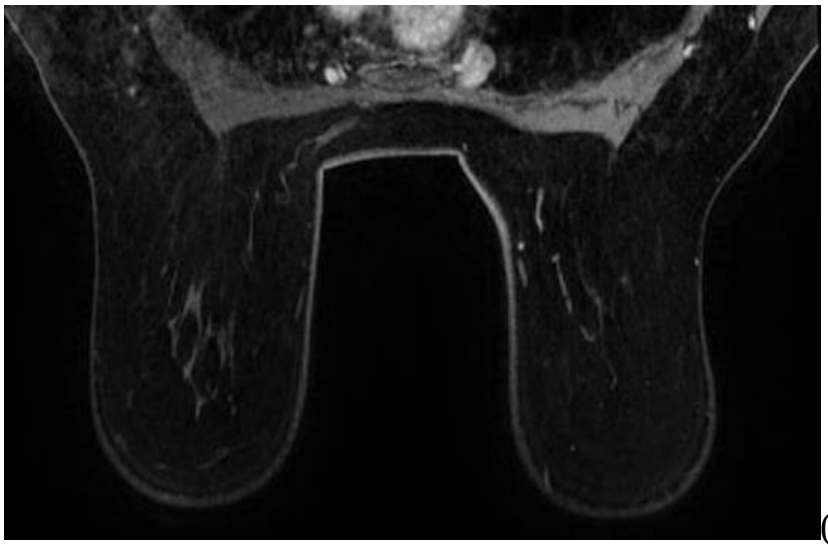
2.9.2.4 Pathological Correlates:

The majority of DW-MRI performed clinically to date has focused on the measurement of extracellular water diffusion. In tissues, the random paths extracellular water molecules may otherwise take are hindered by structural interfaces. In a highly cellular tissue, extracellular water would not be able to diffuse far during the MR observation period without being blocked by cell membranes; this would lead to a short diffusional path and a reduced ADC. Conversely, in cystic or necrotic portions of tumours with fewer structural barriers present, the diffusional path-length would be associated with a high ADC value.

ADC maps, derived from diffusion-weighted imaging, can therefore provide a non-invasive measure of cellularity. (Herneth AM,et al 2003) In terms of oncological imaging this has obvious potential for diagnosis, treatment planning and monitoring. (Paran Y, et al 2004).

2.9.2.5 Breast Diffusion Weight Image MRI:

has been applied to diagnose breast cancer and identify cancer extension (Woodhams R el at, 2005) and (Sekiguchi R et al, 2004) .Isotropic DW-MRI performed with echo-planar sequences (b-values 0, 750 and 1000s/mm2) showed that the mean ADC value of breast cancer was 1.12+/ −0.24×10−3mm2/s, which was lower than that of normal breast tissue, and that the sensitivity of the ADC value for breast cancer using a threshold of less than 1.6×10−3mm2/s was 95%. Also, the ADC value for invasive ductal carcinoma was lower than that of noninvasive ductal carcinoma. Seventy-five percent of all cases showed precise distribution of low ADC value as cancer extension (Guo Y el at, 2002.). Also confirmed that DW-MRI may be potentially useful in distinguishing between malignant and benign breast lesions. Further, tumour cellularity has a significant influence on the ADCs obtained in both benign and malignant breast tumours. Limitations of the technique in the breast arise from underestimation of ADC, primarily due to susceptibility artifact from blood products and the limit of spatial resolution. (Guo Y el at, 2002).


(A)

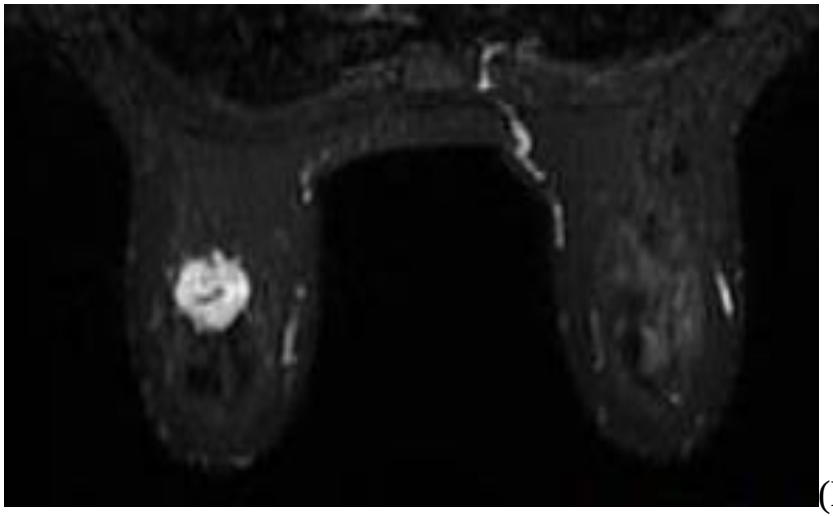

(B)

Figure 2-26. (A)Normal MRI breast, (B)hyperintense lesion (http://mammoguide.com/)

2.9.2.6 Temporal Resolution-Kinetic Analysis of the Signal Intensity Time Curves:

Lesion enhancement is described as homogeneous, heterogeneous, rim enhancement, or enhancement with dark internal septations. (Kuhl et al., 1999)

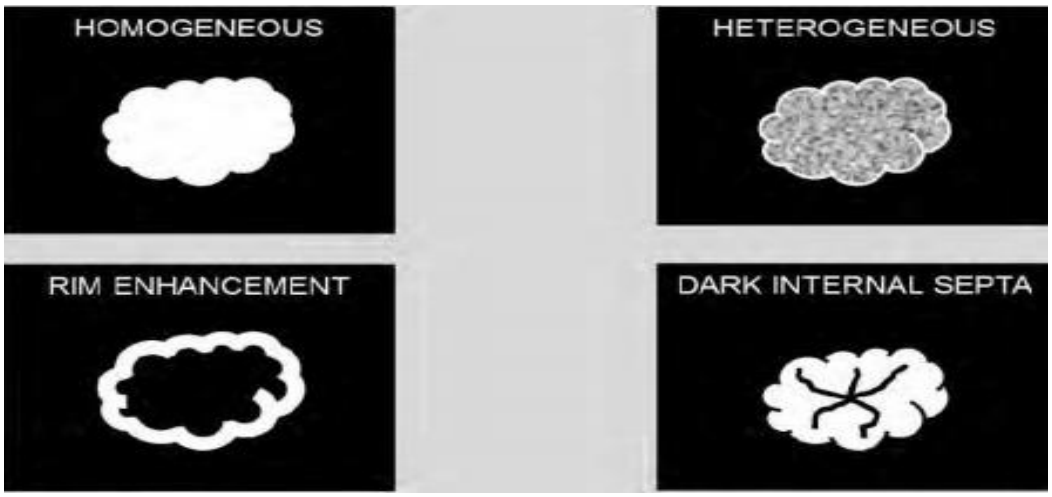


Figure 2-27.Proper terminology (according to the BI-RADS lexicon for lesions enhancement patterns) homogeneous, heterogeneous, rim enhancement, and enhancement with dark. (http://cdn.intechopen.com/pdfs-wm/32005.pdf)

The relative enhancement of breast lesions was assessed by drawing a region-of-interest in the lesion itself. The enhancement was then calculated according to the following formula: Relative signal enhancement (%) = (SIpost – SIpre) / SIpre x 100 In this formula, SIpre and SIpost represent pre-contrast and post-contrast signal intensities, respectively. By calculating the signal intensity time curves, it was demonstrated that enhancement patterns can be divided into two phases: early enhancement (from contrast administration to approximately two minutes post-contrast, or when the curve starts to change), followed by the delayed enhancement (Marc Lobbes et al, 2012).

2.9.2.6.1 Mass Enhancement Occurs in Six Main Patterns:

Homogeneous enhancement is uniform and confluent enhancement throughout the mass, Heterogeneous enhancement is nonuniform enhancement, which varies within the mass, Rim enhancement is enhancement mainly concentrated at the periphery of the mass. This type of enhancement is frequently a feature of high-

grade invasive ductal cancer, fat necrosis, and inflammatory cysts. A lesion with rim enhancement that is not a typical cyst has a 40% chance of malignancy, Dark internal septations refers to non-enhancing septations in an enhancing mass. These are typical for fibroadenomas, especially when the lesion has smooth or lobulated margins, Enhancing internal septations are usually a feature of malignancy, Central enhancement is pronounced enhancement of a nidus within an enhancing mass. Central enhancement has been associated with high-grade ductal cancer. Central enhancement has been associated with high-grade ductal cancer (K. J. Macura et al November 1, 2006).

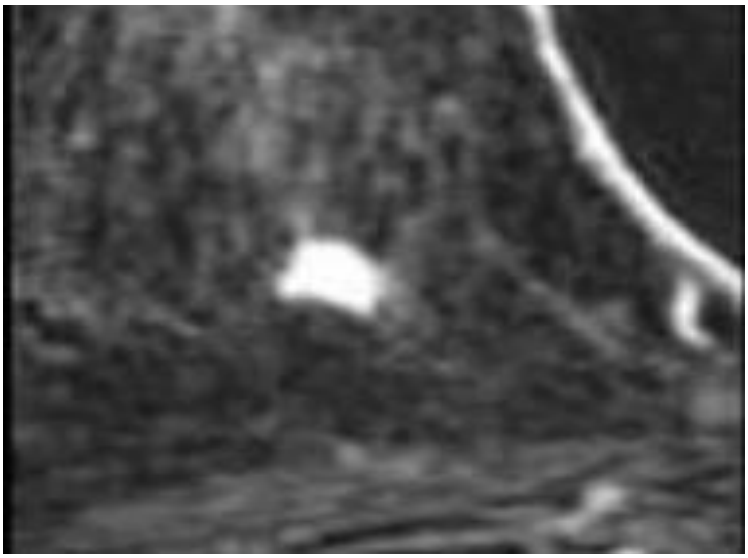


Figure2-28. Invasive ductal carcinoma with Homogeneous enhancement (http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html)

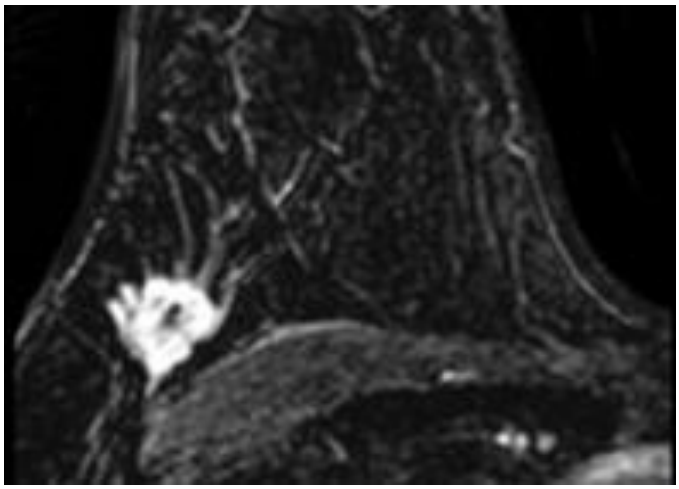
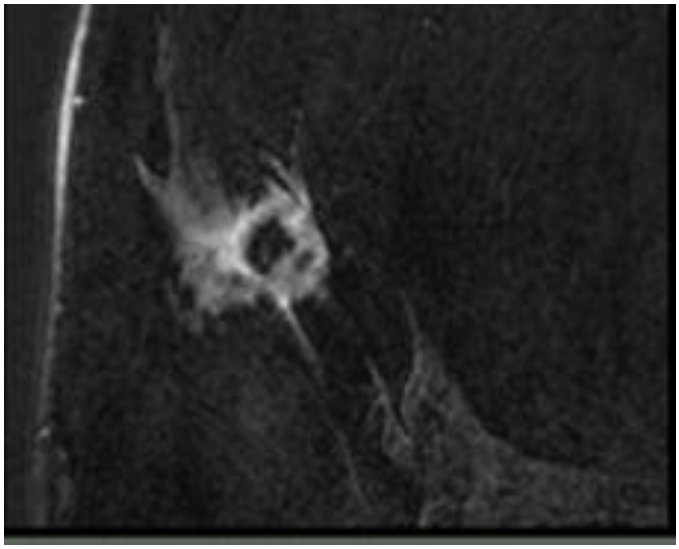


Figure2-29.invasive lobular carcinoma with hetergenous enhacement

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html



Figuer2-30.invasive ductal carcinoma with rim enhancement.

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html

2.9.3.6.2 The Kinetic analysis Take About Six Minutes Repetitive Scanning in Total and can lead to Three Types of Curve:

First we look at the initial upslope of the curve during the first one to two minutes. This is either slow, medium or rapid.
Then there is the delayed portion - two minutes or more after the injection of contrast.
This part of the curve shows either an increase, plateau or washout. (K. J. Macura et al November 1, 2006).

Type 1

There is a slow rise and a continued rise with time. A lesion with a type 1 curve has a chance of 6% of being malignant. (K. J. Macura et al November 1, 2006).

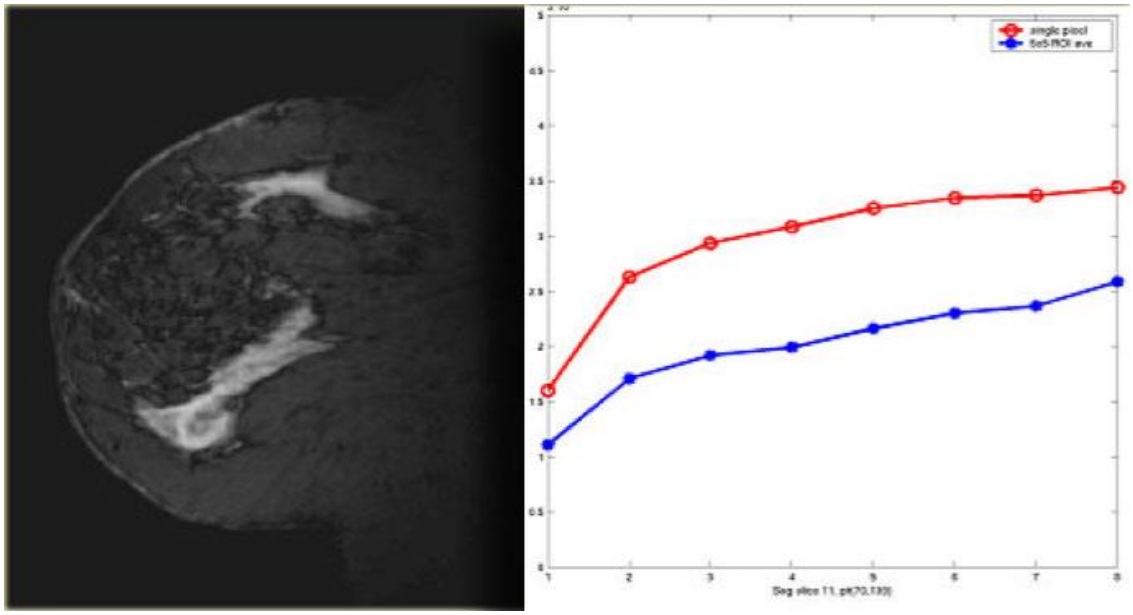


Figure2-31.Type 1enhancement curve

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html

Type 3

The type 3 curve shows a rapid initial rise, followed by a drop-off with time (washout) in the delayed phase. A lesion with this type of curve is malignant in 29-77%.

This is the red on the Computer Aided Detection (CAD). (K. J. Macura et al November 1, 2006).

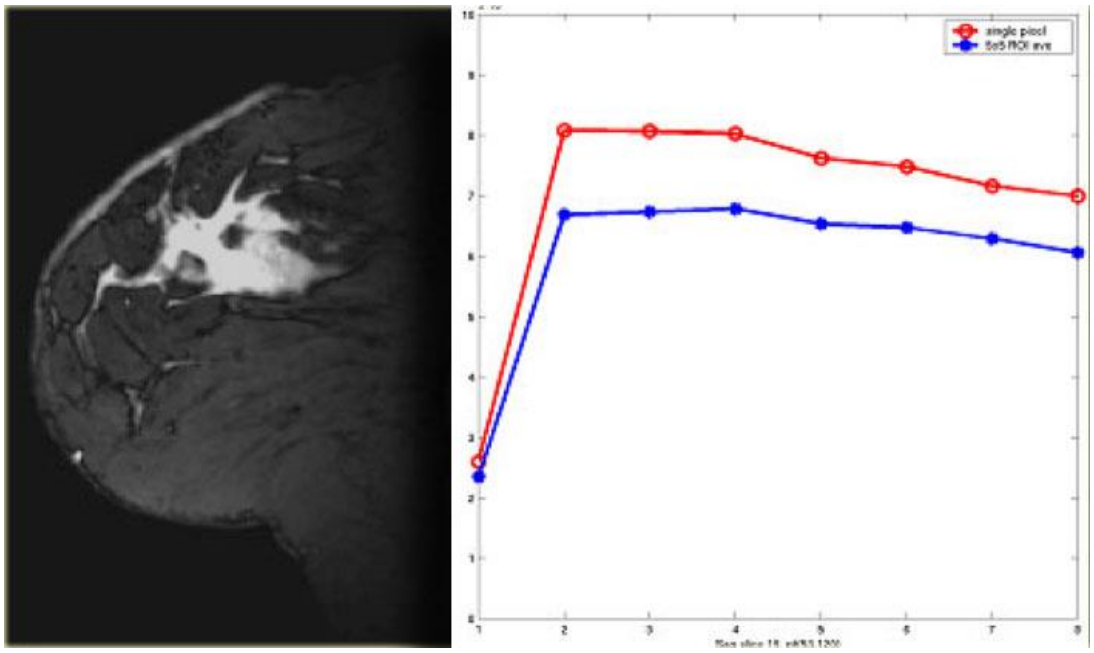


Figure2-32. Type 3 enhancement curve

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html).

Type 2

Then there is the type 2 curve, which is in the middle: a slow or rapid initial rise followed by a plateau in the delayed phase, which is allowed a variance of 10% up or down. The chance of a lesion with a type 2 curve being malignant lies somewhere between the 6% of the type 1 curve and the 29-77% of the type 3 curve.

Many physicians will biopsy lesions with type 2 curves.

For non-mass enhancement, kinetics are not very useful. (K. J. Macura et al November 1, 2006).

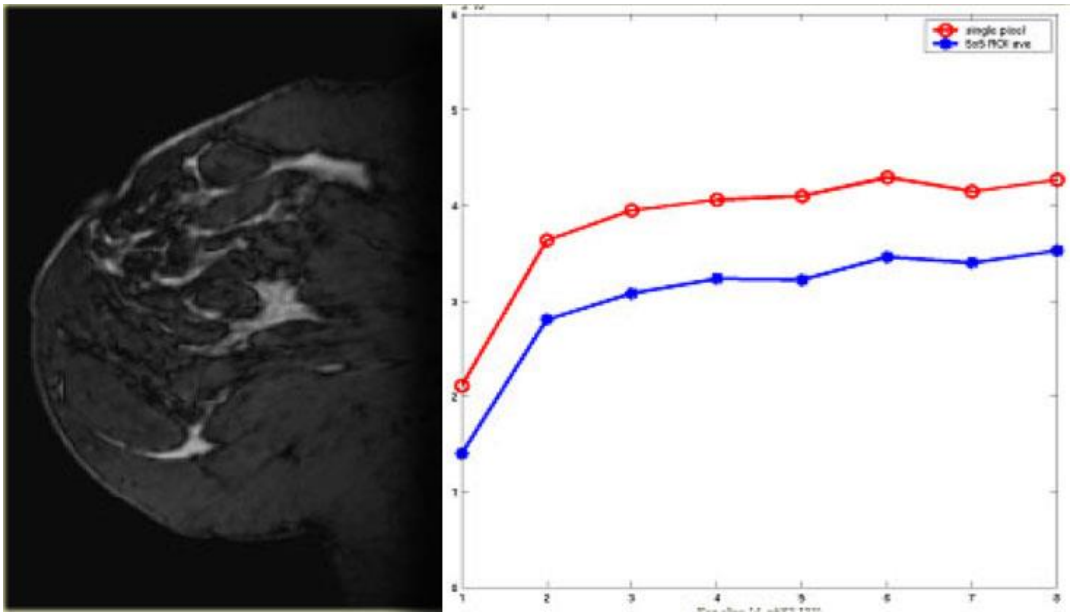


Figure2-33.Type2 enhancement curve

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html

2.9.3.6.3 Computer Aided Detection (CAD):

Computer Aided Detection is a purely kinetic evaluation. It does not evaluate the anatomy or pathology of the images. CAD when referenced to MRI is not a computer software system that provides a second reading of the study. What CAD-MRI does is provides the radiologist with additional tools that analyze enhancement kinetics of malignancy. It improves detection in the initial reading of the MRI scan through lesion detection and differentiation and lesion kinetics qualification. One of the most important indicators of malignancy using contrast enhanced breast MR imaging is the “wash in, progression, and wash out times.” CAD looks at the curves and peak enhancements for the contrast (automated kinetics) about 90-120 seconds, which is

the wash in time. How long it takes to disperse or its pattern of dispersal is the washout time (Nicholas Joseph, 2006).

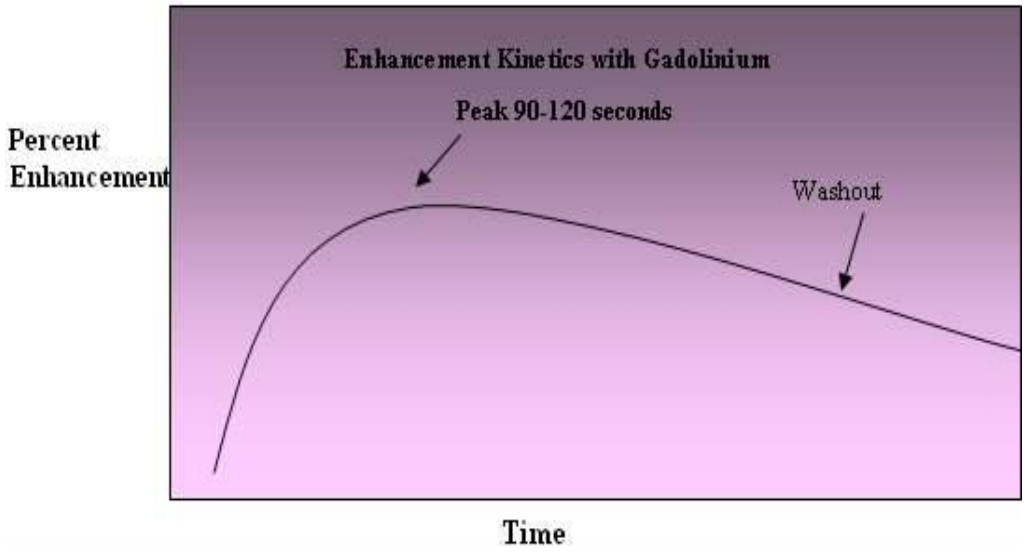


Figure2-34 .Contrast enhancement peaks at about 90-120 seconds, which is the wash in time. (Nicholas Joseph, 2006).

It also has some very nice features, including motion registration during subtraction, which can correct for a patient's movement during the exam something not all MRI scanners can do. It can do multi planar reconstruction and subtraction very well and very quickly it also has a good measurement package. In CAD, red is bad: it means type 3 washout, and probably cancer (Katarzyna J. Macura et al 2006)

The CAD has detected some very small areas with type 3 washout (in red). When you look at CAD images, take note of the worst (red) areas. This was a large invasive ductal carcinoma. (Katarzyna J. Macura et al 2006)

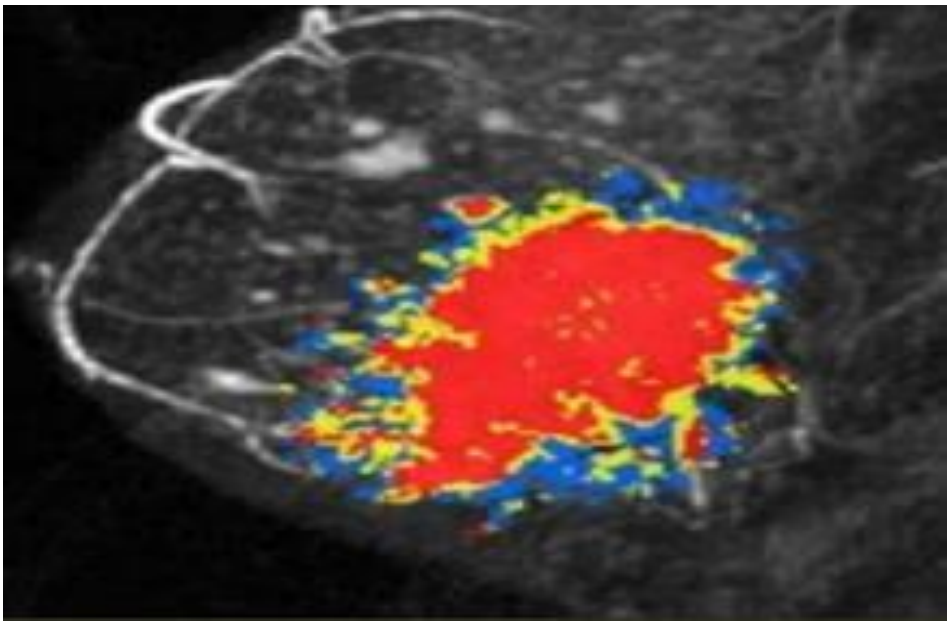


Figure 2-35.CAD with a large of type 3 enhancement

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html

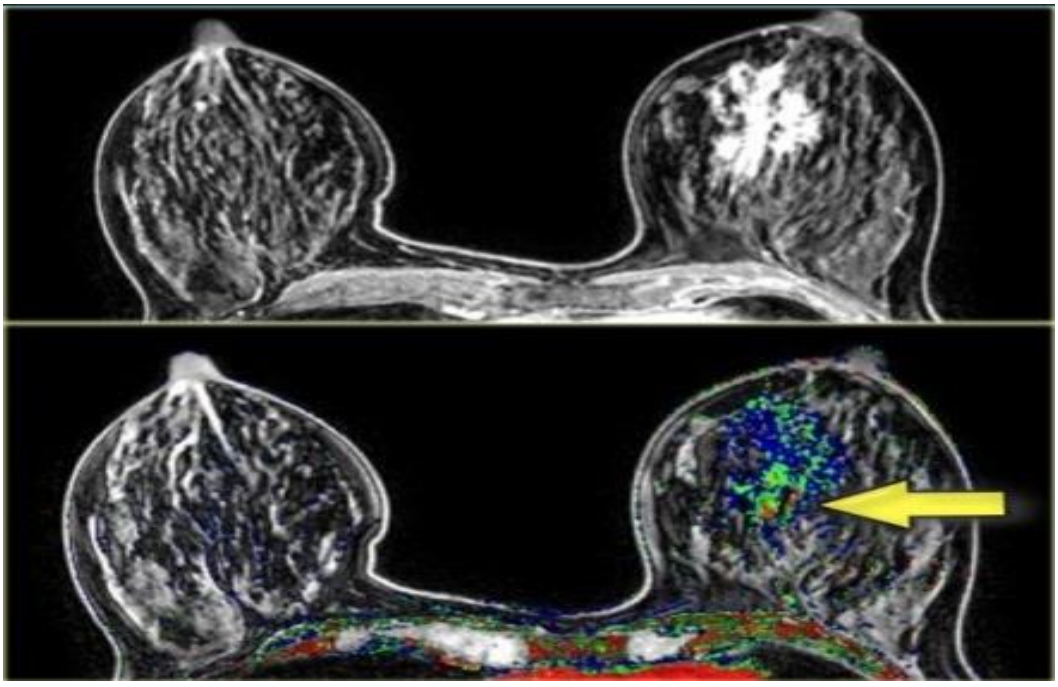


Figure3-36. Very small areas with type 3 washout (in red).

http://www.radiologyassistant.nl/en/p47a585a7401a9/breast-mri.html

The enhancement kinetics of tumors using CAD is as follows: rapid early enhancement that continues to progress exhibit Type I enhancement kinetics and are considered benign. Tissue having Type I kinetics is colored blue with CAD. An area displaying rapid early enhancement that levels off or plateaus has Type II kinetics. The pathology of a Type II lesion is indeterminate; CAD colors these lesions yellow (some CAD programs use green). A tumor or area with Type III kinetics will have rapid "wash in" and rapid washout of contrast. Type III kinetics within a tumor is colored red to indicate an area of cancerous growth. Type III kinetics is seen in 60% of cancers making all Type III tumors suspicious and should be further evaluated with biopsy. Kinetic assessment of tumors seen on MRI is a basic part of the imaging profile along with tumor morphology assessment. Enhancement kinetics alone is not a conclusive standard for evaluating MRI displayed tumors. The basis for this is that at least 6% of malignant tumors display Type I enhancement kinetics. The caution here is for the radiologist to weigh each tumor's enhancement kinetics against strict morphology standards. About 34% of Type II enhancement kinetic tumors are found to be malignant at biopsy, and 60% of Type III proves malignant at biopsy. What we have learned from using CAD in MR breast imaging diagnosis is that it is not the ultimate diagnostic tool because of the statistical overlap between malignant and benign tumor kinetics. But when buffered with morphological analysis and radiologist experience even what appears to be a benign tumor can be diagnosed when it is small. Diagnosis therefore should error in favor of biopsy or short interval follow-up imaging for morphologically suspicious Type I and Type II tumors. This will help insure the patient suffers no adverse consequence of an under read MRI. .(Nicholas Joseph,2006).

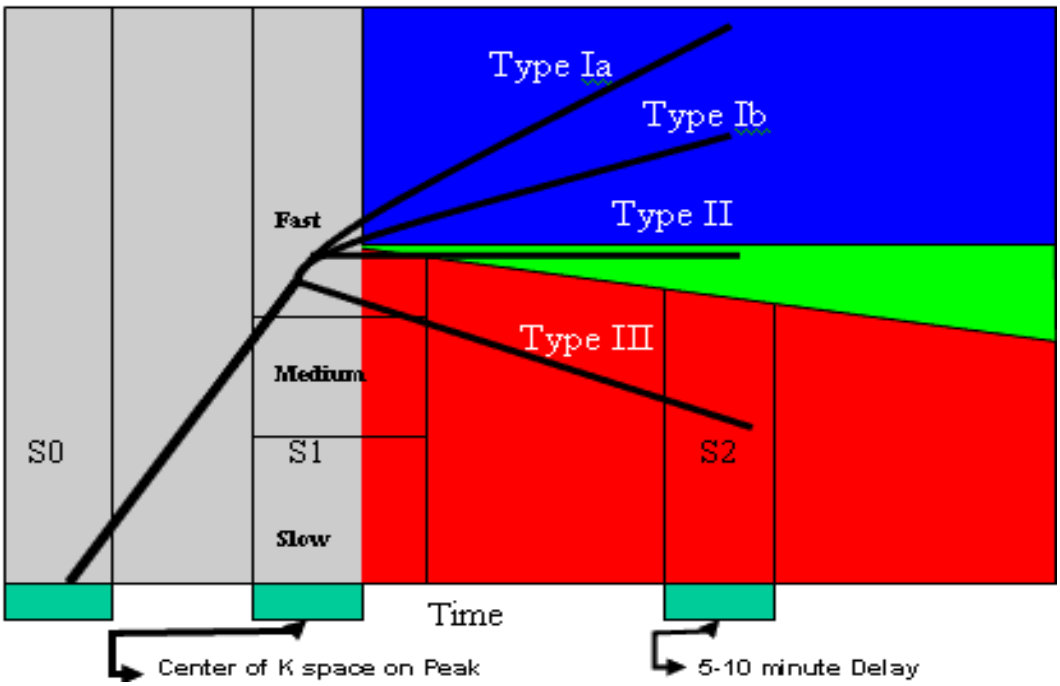


Figure2-37.This diagram demonstrates the enhancement kinetics following gadolinium injection for breast cancer imaging. Type I (blue); Type II (green); Type II (red)I (Nicholas Joseph,2006).

The statistical ability to detect breast lesions using magnetic resonance imaging with CAD is shown in the two tables (2-4) and (2-5) below (Nicholas Joseph, 2006):

Table2-4 .CAD with biopsy

https://www.ceessentials.net/article40.html

Percent of CAD Localized Tumors Correlated by Biopsy		
	Malignant	Benign
Type I	6	83
Type II	34	11.5
Type III	60	5.5

Table 2-5 breast cancer in dense breast

https://www.ceessentials.net/article40.html

Breast Cancer Detection in Dense Breast Tissue			
	MRI	Mammography	Ultrasound
(Cancer size or extent) Underestimated	12	37	40
Sensitivity	98	83	71
Multifocal or Multicentric Detected	100	35	30

2.10 Previous Studies:

(J. Magn, 2002) evaluated the value of diffusion-weighted imaging (DWI) in distinguishing between benign and malignant breast lesions. Results was the ADCs varied substantially between benign breast lesions ((1.57 ± 0.23) × 10^{-3} mm^2/second) and malignant breast lesions ((0.97 ± 0.20) × 10^{-3} mm^2/second). In addition, the mean ADCs of the breast lesions correlated well with tumor cellularity ($P < 0.01$, $r = -0.542$). Conclusion was the ADC would be an effective parameter in distinguishing between malignant and benign breast lesions. Further, tumor cellularity has a significant influence on the ADCs obtained in both benign and malignant breast tumors.

(Mieke Kriege et al Med 2004) they were studies Efficacy of MRI and Mammography for Breast-Cancer Screening in Women with a Familial or Genetic Predisposition.

They screened 1909 eligible women, including 358 carriers of germ-line mutations. Within a median follow-up period of 2.9 years, 51 tumors (44 invasive cancers, 6 ductal carcinomas in situ, and 1 lymphoma) and 1 lobular carcinoma in situ were detected. The sensitivity of clinical breast examination, mammography, and MRI for detecting invasive breast cancer was 17.9 percent, 33.3 percent, and 79.5 percent, respectively, and the specificity was 98.1 percent, 95.0 percent, and 89.8 percent, respectively. The overall discriminating capacity of MRI was significantly better than that of mammography ($P<0.05$). The proportion of invasive tumors that were 10 mm or less in diameter was significantly greater in our surveillance group (43.2 percent) than in either control group (14.0 percent [$P<0.001$] and 12.5 percent [$P=0.04$], respectively). The combined incidence of positive axillary nodes and micrometastases in invasive cancers in our study was 21.4 percent, as compared with 52.4 percent ($P<0.001$) and 56.4 percent ($P=0.001$) in the two control groups .conclusions were MRI appears to be more sensitive than mammography in detecting tumors in women with an inherited susceptibility to breast cancer.

(J. Magn et al, 2002)had one study about to investigate the potential of apparent diffusion coefficients (ADCs) in characterizing breast lesions in vivo. Materials and Methods were two diffusion-weighted (DW) sequences were implemented on a 1.5 Tesla scanner, with low b-value orthogonal and high b-value tetrahedral sensitized sequences. The orthogonal sequence was evaluated on 16 normal volunteers and 23 patients with known lesion types (six benign and 17 malignant). The tetrahedral sequence was evaluated on a smaller number of subjects: two

normal, two malignant, and two benign. Results were the mean value of the ADC of the malignant tumors was reduced compared to that of the benign lesions and normal tissue. This finding was related to the increased cellularity of the malignant lesions. The ADC values were elevated for all tissue types with the low b-value sequence as compared to the high b-value sequence, indicating contributions from perfusion effects at the low b-values. Conclusion were the study clearly shows that DW-MRI can help characterize breast lesions in vivo.

(Savannah C. Partridge et al, 2009) had done study the utility of diffusion-weighted MRI in differentiating benign from malignant breast lesions by assessing the best b values. Result was the mean ADC value was significantly lower for malignant lesions compared to benign lesions ($p < 0.0001$) in all b value combinations. No statistical difference was seen between the ADC obtained from different b value combinations ($p = 0.2581$) in the differentiation between benign and malignant lesions. The ADC calculated from b 0 and 750 s/mm2 was slightly better than the other b value combinations, showing a sensitivity of 92.3% and a specificity of 96.2%.conculison was diffusion-weighted imaging is a potential resource as a coadjutant of MRI in the differentiation between benign and malignant lesions. Such imaging can be performed without a significant increase in examination time, especially because it can be done with lower b values.

(Lalitha Palle et al, 2009) they were study Role of diffusion MRI in characterizing benign and malignant breast lesions. Result wasTwo hundred and eighty breast lesions were detected in our sample of 200 patients. Based on previous experience, lesions with ADC values in the range of $0.89 \pm 0.18 \times 10^{-3}\ mm^2/s$ were called malignant and those between $1.41 \pm 0.56 \times 10^{-3}\ mm^2/s$ were called benign. For normal breast parenchyma, the ADC values were between 1.59 and 1.7 x 10^{-}

$^{3}mm^{2}$/s. Of the 280 lesions, 208 lesions were categorized as benign and 72 lesions were categorized as malignant using these ADC values. Two lesions whose ADC values were in the benign range turned out to be malignant after surgery. Both these lesions also showed type 2 curves on the dynamic contrast-enhanced study. According to this study, the sensitivity of ADC values for the detection of malignant lesions was 97.22% and the specificity was 100% and the positive predictive value was 100% and the negative predictive value was 99%.conculsion was based on our preliminary data, we have found that DWI for breast lesions can differentiate benign from malignant lesions with a high sensitivity and specificity. The usefulness of this technique needs to be further evaluated with larger double-blind studies.

Chapter Three

Material and Method

3.1 Material:

3.1.1 Patients:

The study population was adult women presenting to the radiology department in Dr Suliman Al Habib medical center –Olaya during the period from Jun 2013 to July 2014. It includes 50 patients between the ages of 26 and 80 years (mean age: 41.78 ± 12.48 years). Of these 50 patients, 18 underwent breast MRI with ultrasound, mammography and biopsy. 21 patients underwent breast MRI, ultrasound and mammography .28 patients underwent MRI and biopsy.

3.1.1.1 Inclusion Criteria:

Patient collaborator, Patient weighed less than 120 kg and normal level of creatinine (kidney function).

3.1.1.2 Exclusions Criteria :

Phobia indoor, Patient with mastectomy.

3.1.2 Imaging Tools:

3.1.2.1 MRI Machine:

MRI machine GE HD x1.5 T and coil 8-channel breast array (figuer3-1), (figure 3-2) and (figure3-3).

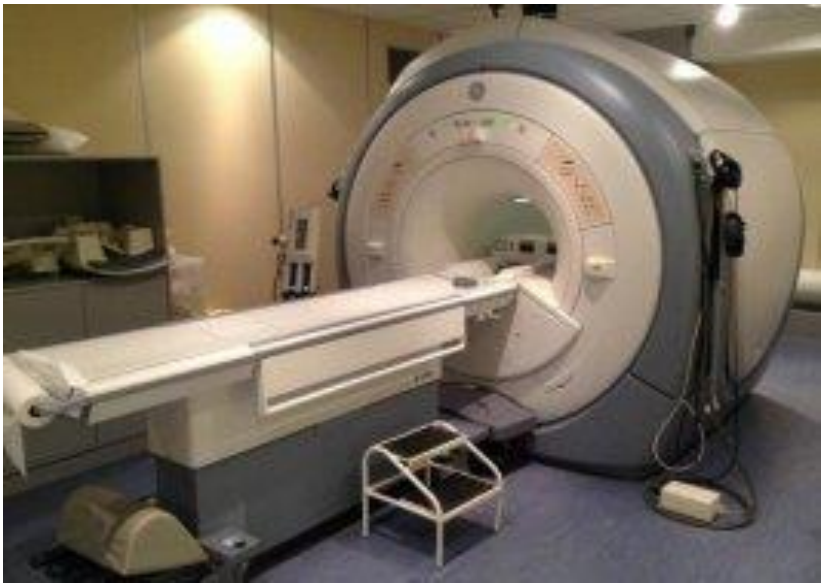


Figure3-1.MRI HD X 1.5T

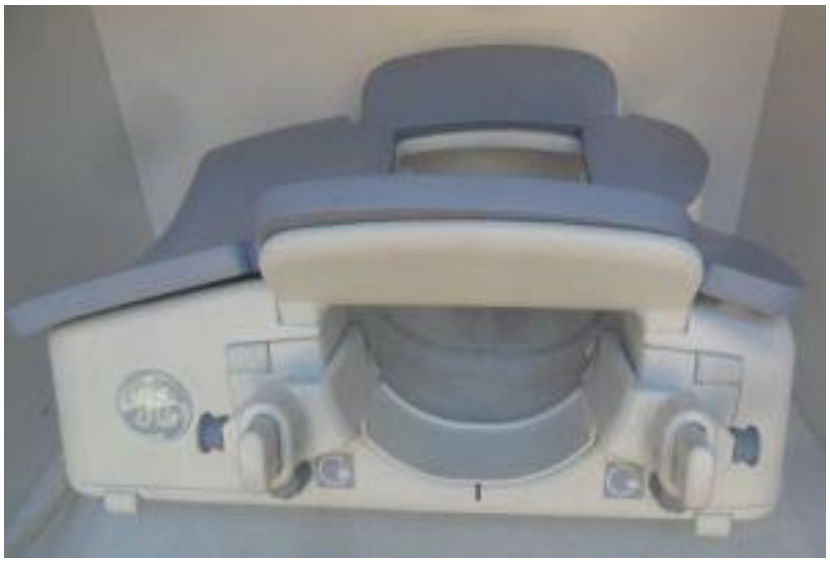


Figure3-2. Coil 8-channel breast array coil

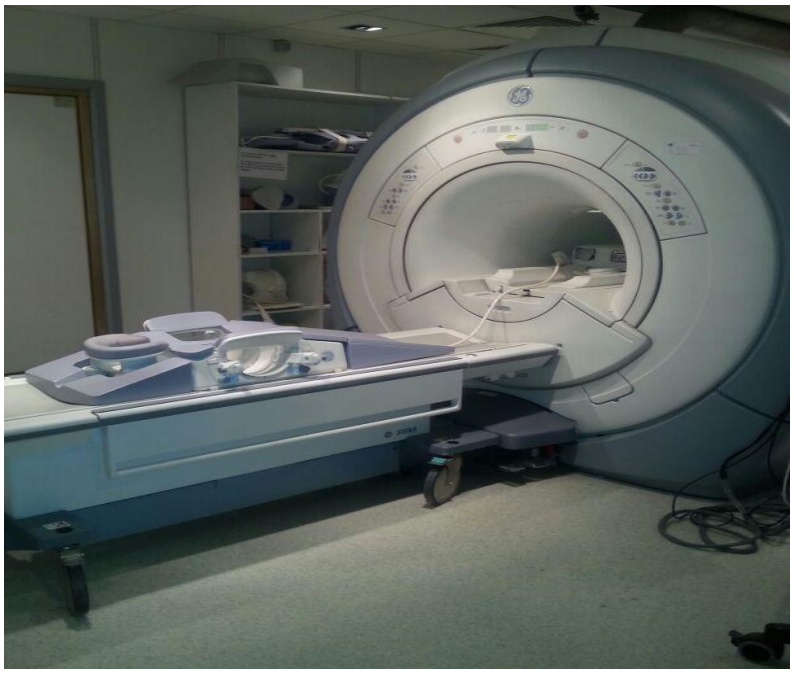


Figure3-3 MRI machine include coil

3.1.2.2 Ultrasound of the Breast:

Ultrasound machine GE LOG IQ9.

Figure3-4. Ultrasound Machine

3.1.2.3 Mammogram:

GE Senographe Essential Digital Mammogram Machine

Figure3-5mammogram machine

3.1.2.4 Histopathology Tools :

There are two types of biopsies of that are performed: fine needle aspiration, and true cut.

In fine needle aspiration Slides, gathering the needle and syringe, methanol and jars. and in true cut need cuter , bradmagnom and formaline

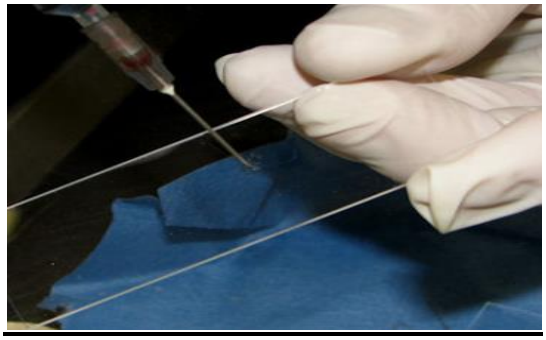


Figure3-6.Slid of FNA

3.2 Methods:

3.2.1 MRI Technique Used

3.2.1.1 Patient Handling:

Immediately prior to the examination, patients put on a gown and pants to prevent possible metallic artifacts from their clothing and to enable more comfortable positioning. The technologist tells the patient of the approximate duration of the scan and the importance of keeping still during image acquisition. The patient is informed that she can communicate with the technologist via the intercom. She is also provided ear plugs to protect against noise created by the gradients.
A dedicated breast coil should be used for breast MRI.

3.2.1.2 Patient Positioning:

The patient is placed in a prone position on the breast coil with a cushion placed under her head. The arms are positioned at the sides of the body or above the head. One possible disadvantage is that the axillary tail of each breast may not be fully covered by the breast coil. These coils usually consist of a multichannel coil (nowadays up to 32-channel) with two loops in which the breasts are placed.

Ensure that each breast hangs as deeply as possible within the coil opening with the nipples centered and pointing straight down.

3.2.1.3 Image Protocol:

Scout images, T2 = TR 5000-2000 , TE 97-85 , ETL 16 , FA 90.0, T1= TR 7000-6000 , TE 10-9 , ETL 3 , FA 90.0, DWI = TR 7000-6000 , TE 76-74 , FA 90.0, Slice Thickness (ST) =5mm, Slice Space (SP) =1mm, Axial T2 with fat suppression, Sagittal T1 3D, Sagittal T2 with fat suppression, Axial DWI using b = 1000 sec/mm2 to improve specificity, Precontrast axial 3D T1 with fat suppression, Post contrast axial dynamic multiphase 3D T1 sequence with fat-suppression (6 acquisitions), Axial 3D T1 with fat suppression, , and Sagittal 3D T1 with fat suppression.

3.2.1.4 The Time and Intravenous Contrast:

We were giving gadolinium DTPA 20ml by intravenous.

3.2.2 Method of Interpretation:

T1, T2, DWI, contrast enhancement, Curve, Bi-rads, size of lesion in MRI and ultrasound, Doppler in ultrasound and mammogram were applied. Images were diagnosed by radiologist. Histology result was taking from laboratory department. Patient age and history were taking from patient file in hospital.

3.2.3 Variables:

The study of population will be assessed against the following variables :patient age , Clinical history , family history ,(DWI) ,Ultrasound , Mammography , Creatinine test ,T1 Post contrast MR , Dynamic Curve MRI, Bi-rads of MRI , lesions shape in DWI and histopathology.

3.2.4 Source of Data Collection:

1-the history of the patients

2-medical report of ultrasound, mammography, MRI, and histopathology.

3.2.5 Statistical Analysis:

All data were presented as mean ± SD values. Data were analyzed by an independent *t* test and by correlation analysis with the use of the SPSS (Inc., Chicago, Illinois version 16). A value of *P* 0.05 was considered significant.

3.2.6 Ethical consideration:

-No identification or individual details were published.

-No information or patient details will be disclosed or used for reasons other than the study.

Chapter Four

Results

4.1 General Characteristics of the Sample:

4.1.1 Age Distribution:

The following tables show the studied patients: 50 females presented with 50 breast lesions.

Table (4-1) Statistical Description of the sample age:

Statistical Description of the sample age/Years	
Mean	41.78
Median	39.50
Std. Deviation	±12.48
Minimum	26.00
Maximum	80.00
Total Sample Number	**50**

Table (4-2) Classification of Sample according to age, Frequency and Percentages:

Age	Frequency	Percentages%
26-40	28	56.0
41-55	15	30.0
56-75	6	12.0
76+	1	2.0
Total	**50**	**100.0**

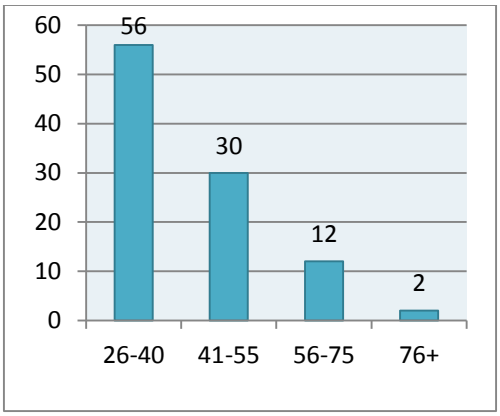


Figure (4-1) Classification of Sample according to age.

4.2 MRI Results and Correlations:

Table (4-3): MRI Diagnoses and Classification of 50 Breast Lesions:

	MRI Classification of Breast Lesion		
MRI Diagnoses/Findings	**Benign**	**Malignant**	**Total**
Suspicious Breast Masses	0	5	5
Hematoma	1	0	1
Cyst	1	0	1
Degeneration	1	0	1
Fibro Adenoma	13	0	13
Fat Necrosis	4	0	4
Fibrocystic Change	8	0	8
Infiltrating Ductal Carcinoma	0	9	9
Intraductal Papillary Cancer	0	1	1
Myxoid Fibroid	2	0	2
Papilloma	3	0	3
Pseudoangiomatous Hyperplasia	1	0	1
Popcorn Calcification	0	1	1
Total	34	16	50

Table (4-4): MRI Diagnoses and Classification of 50 Breast Lesions According to Age Classes:

		Age Classes/Years				Total
		26-40	41-55	56-75	>76	
MRI Diagnosis	Benign Lesions	21	6	1	0	28
	Malignant Lesions	7	9	5	1	22
Total		28	15	6	1	50
P- Value =0.002 <0.05						

Table (4-5) Cross tabulation between the patients signs and symptoms and MRI Diagnosis (Benign and Malignant):

			Clinical Signs and Symptoms						Total
			Mass	Mass/Pain	Pain	Discharge Nipple	Check Up	Mass/ Discharge Nipple	
MRI	Benign	Count	14	1	5	5	3	0	28
		% of Total	28.0%	2.0%	10.0%	10.0%	6.0%	.0%	56.0%
	Malignant	Count	4	4	6	4	3	1	22
		% of Total	8.0%	8.0%	12.0%	8.0%	6.0%	2.0%	44.0%
Total		Count	18	5	11	9	6	1	50
		% of Total	36.0%	10.0%	22.0%	18.0%	12.0%	2.0%	100.0%
Pearson Chi-Square7.95.Correlation is significant at p<0.005 Sig. 0.159									

Table (4-6): Analysis of Magnetic Resonance Images of the 50 Breast lesions signals intensity in T_1, T_2, and DWI Techniques:

Classification	NO	Signal Intensity at T_1Weighted Imaging	Signal Intensity at T_2Weighted Imaging	Signal Intensity at Diffusion Weighted Imaging DWI
Suspicious Breast Masses	5	1=hyperintense 4=hypointense	3=hyperintense 2=hypointense	5=isointense
Hematoma	1	1=hyperintense	1=hyperintense	1=hyperintense
Cyst	1	1=hypointense	1=isointense	1=hyperintense
Degeneration	1	1=hypointense	1=hypointense	1=isointense
Fibro Adenoma	13	13=hypointense	8=hyperintense 3=hypointense 2=isointense	13=hyperintense
Fat Necrosis	4	4=hyperintense	4=hyperintense	4=hypointense
Fibrocystic Change	8	2=hyperintense 6=hypointense	8=hyperintense	7=hyperintense 1=hypointense
Infiltrating Ductal Carcinoma	9	8=hypointense 1=isointense	3=hyperintense 5=hypointense 1=isointense	4=hyperintense 4=hypointense
Intraductal Papillary Cancer	1	1=hypointense	1=isointense	1=hyperintense
Myxoid Fibroid	2	2=hypointense	2=hyperintense	2=hyperintense
Papilloma	3	2=hyperintense 1=hypointense	2=hyperintense 1=hypointense	2=hyperintense 1=hypointense
Pseudoangiomatous Hyperplasia.	1	1=hypointense	1=isointense	1=isointense
Popcorn Calcification	1	1=hypointense	1=hypointense	1=isointense
Statistical Correlations	50	***(Pearson Chi-Square =48.5) P- Value =0.118 >0.05***	***(Pearson Chi-Square =58.8) P- Value =0.017 <0.05***	***(Pearson Chi-Square =84.9) P- Value =0.000 <0.05***

Table (4-7): Analysis of Magnetic Resonance Images of the 50 Breast lesions in Dynamic Curve and BI-RAD Techniques:

Classification	No	Dynamic Curve			BI-RAD			
		1.0	2.0	3.0	2.0	3.0	4.0	5.0
Suspicious Breast Masses	5	-	-	5	-	1	2	2
Hematoma	1	1	-	-	-	1	-	-
Cyst	1	1	-	-	-	1	-	-
Degeneration	1	1	-		-	1	-	-
Fibro Adenoma	13	11		2	-	13	-	-
Fat Necrosis	4	2	2	-	1	2	1	-
Fibrocystic Change	8	7	1	-	-	7	1	-
Infiltrating Ductal Carcinoma	9	-	-	9	-	5	1	3
Intra Ductal Papillary Cancer	1	-	-	1	-	-	1	-
Myxoid Fibroid	2	2	-		-	2	-	-
Papilloma	3	2	-	1	-	3	-	-
Pseudoangiomatous Hyperplasia.	1	1	-	-	-	-	1	-
Popcorn Calcification	1	1	-	-	-	1	-	-
Total Lesions	**50**	**29**	**3**	**18**	**1**	**37**	**7**	**5**
		Pearson Chi-Square=55.6 P- Value =0.032 <0.05			***Pearson Chi-Square =73.53 P- Value =0.069 >0.05***			

Table (4-8): Morphologic Characteristics of 50 breast Lesions in DWI:

	Morphologic Characteristics in DWI		Total
	Irregular	Regular	
Suspicious Breast Masses	5	0	5
Hematoma	0	1	1
Cyst	0	1	1
Degeneration	0	1	1
Fibro Adenoma	0	13	13
Fat Necrosis	2	2	4
Fibrocystic Change	2	6	8
Infiltrating Ductal Carcinoma	7	2	9
Intra Ductal Papillary Cancer	1	0	1
Myxoid Fibroid	1	1	2
Papilloma	2	0	2
Pseudoangiomatous Hyperplasia	1	0	1
Popcorn Calcification	0	1	1
Total	22	28	50
	44.0%	56.0%	100.0%
(Pearson Chi-Square =35.11)	***P- Value =0.014 <0.05***		

Table (4-9): MRI contrast enhancement of the breast lesions cross tabulated with MRI diagnosis results:

		MRI FINDINGS		Total
		Benign Lesions	Malignant Lesions	
MRI Contrast Enhancement of Lesions	**Intermediate**	16	1	17
	Slow	10	5	15
	Strong	2	16	18
	Total	28	22	50
P –value = 0.000				

Table (4-10): Cross Tabulation between the Histological Results and MRI Findings:

		HISTOPATHOLOGY FINDINGS		Total
		Benign Lesions	Malignant Lesions	
MRI Findings	Benign Lesions	12	5	17
	Malignant Lesions	2	9	11
Total		14	14	28
(Pearson Chi-Square =443.9) P- Value =0.002 <0.05				
Sensitivity=82%, Specifity=71%, Accuracy=75% and Positive Predictive Value (PPV) =64%				

Table (4-11): Cross Tabulation between the MRI Findings and BIRAD Results

			BIRAD					Total
			0.00	2.00	3.00	4.00	5.00	.00
MRI Findings	Benign	Count	0	1	25	2	0	28
		% of Total	.0%	2.0%	50.0%	4.0%	.0%	56.0%
	Malignant	Count	1	0	11	5	5	22
		% of Total	2.0%	.0%	22.0%	10.0%	10.0%	44.0%
Total		Count	1	1	36	7	5	50
		% of Total	2.0%	2.0%	72.0%	14.0%	10.0%	100.0%
Correlation is significant at p<0.005 Sig0.010 Pearson Chi-Square13.200								

Table (4-12): Cross Tabulation between the MRI Findings and Dynamic Contrast:

			Dynamic Curve Values				Total
			.00	1.00	2.00	3.00	.00
MRI Findings	Benign	Count	1	23	2	2	28
		% of Total	2.0%	46.0%	4.0%	4.0%	56.0%
	Malignant	Count	2	6	1	13	22
		% of Total	4.0%	12.0%	2.0%	26.0%	44.0%
Total		Count	3	29	3	15	50
		% of Total	6.0%	58.0%	6.0%	30.0%	100.0%
Pearson Chi-Square18.242.Correlation is significant at p<0.005 Sig0.000							

Table (4-13): Cross tabulation between the MRI Diagnosis (Benign and Malignant) and Ultrasound Doppler Flow:

				Ultrasound Doppler Flow			Total
				Few	Free	More	
MRI Findings	Benign	Count	1	5	21	1	28
		% of Total	2.0%	10.0%	42.0%	2.0%	56.0%
	Malignant	Count	4	9	6	3	22
		% of Total	8.0%	18.0%	12.0%	6.0%	44.0%
Total		Count	5	14	27	4	50
		% of Total	10.0%	28.0%	54.0%	8.0%	100.0%
Pearson Chi-Square11.725 , Correlation is significant at p<0.005 Sig. 0.008							

Table (4-14): MRI Contrast Enhancement of the Breast Lesions Cross Tabulated With Histopathology Results:

		HISTOPATHOLOGY FINDINGS			Total
		NA	Benign Lesions	Malignant Lesions	
MRI Contrast Enhancement of Lesions	Intermediate	10	4	3	17
	Slow	5	9	1	15
	Strong	7	2	9	18
Total		22	15	13	50
NA stands for: not applicable					*P* –value = 0.005

Table (4-15): Cross Tabulation between the BI-RAD MRI values with Histological Results:

		BI-RAD MRI				Total
		2.00	3.00	4.00	5.00	
HISTOPATHOLOGY FINDINGS	Benign	1	29	2	0	32
	Malignant	0	7	5	6	18
Total		1	36	7	6	50
P –value = 0.001						

Table (4-16): Cross Tabulation between the MRI dynamic curves with values Histological Results:

		MRI Dynamic Curve			Total
		1.00	2.00	3.00	
HISTOPATHOLOGY FINDINGS	Benign	27	2	3	32
	Malignant	2	1	15	18
Total		29	3	18	50
P –value = 0.000					

Table (4-17): Cross Tabulation between the Lesion Shape at DWI and Histological Results:

			Lesion Shape at DWI		Total
			Irregular	Regular	
Histopathology		Count	7	15	22
		% of Total	14.0%	30.0%	44.0%
	Benign	Count	5	10	15
		% of Total	10.0%	20.0%	30.0%
	Malignant	Count	10	3	13
		% of Total	20.0%	6.0%	26.0%
Total		Count	22	28	50
		% of Total	44.0%	56.0%	100.0%
Pearson Chi-Square7.736. Correlation is significant at p<0.005 Sig. 0.021					

4.3 Ultrasonography Results and Correlations:

Table (4-18): Cross Tabulation between the Doppler Ultrasound Blood Flow and Histological Results:

				Doppler Ultrasound Blood Flow			Total
				Few	Free	More	
Histopathology		**Count**	**1**	**4**	**17**	**0**	**22**
		% of Total	**2.0%**	**8.0%**	**34.0%**	**.0%**	**44.0%**
	Benign	Count	1	5	8	1	15
		% of Total	2.0%	10.0%	16.0%	2.0%	30.0%
	Malignant	Count	3	5	2	3	13
		% of Total	6.0%	10.0%	4.0%	6.0%	26.0%
	Total	Count	5	14	27	4	50
		% of Total	10.0%	28.0%	54.0%	8.0%	100.0%
Pearson Chi-Square15.747 .Correlation is significant at p<0.005 Sig. 0 .015							

Table (4-19): Cross Tabulation between the Ultrasonography Results and Lesion Shape at DWI:

			Lesion Shape at DWI		Total
			Irregular	Regular	
Ultrasonography Findings		**Count**	**4**	**0**	**4**
		% of Total	**8.0%**	**.0%**	**8.0%**
	Benign	**Count**	11	22	33
		% of Total	22.0%	44.0%	66.0%
	Malignant	**Count**	7	6	13
		% of Total	14.0%	12.0%	26.0%
	Total	**Count**	22	28	50
		% of Total	44.0%	56.0%	100.0%
Pearson Chi-Square. 7.126 Correlation is significant at p<0.005 Sig. 0.028					

Table (4-20): Cross Tabulation between the Ultrasonography Results and MRI Contrast Enchantment:

			MRI Contrast Enchantment			Total
			Intermediate	Slow	Strong	
Ultrasonography Findings		Count	0	0	4	4
		% of Total	.0%	.0%	8.0%	8.0%
	Benign	Count	13	12	8	33
		% of Total	26.0%	24.0%	16.0%	66.0%
	Malignant	Count	4	3	6	13
		% of Total	8.0%	6.0%	12.0%	26.0%
Total		Count	17	15	18	50
		% of Total	34.0%	30.0%	36.0%	100.0%
Pearson Chi-Square9.726 Correlation is significant at p<0.005 Sig. 0.045						

Table (4-21): Cross Tabulation between the Ultrasonography Results and BIRAD Results:

			BIRAD					Total
			.00	2.00	3.00	4.00	5.00	
Ultrasonography Findings		Count	0	0	3	1	0	4
		% of Total	.0%	.0%	6.0%	2.0%	.0%	8.0%
	Benign	Count	0	1	26	5	1	33
		% of Total	.0%	2.0%	52.0%	10.0%	2.0%	66.0%
	Malignant	Count	1	0	7	1	4	13
		% of Total	2.0%	.0%	14.0%	2.0%	8.0%	26.0%
Total		Count	1	1	36	7	5	50
		% of Total	2.0%	2.0%	72.0%	14.0%	10.0%	100.0%
Pearson Chi-Square12.530 .Correlation is significant at p<0.005 Sig.0.129								

Table (4-22): Cross Tabulation between the Ultrasonography Results and Dynamic Curve Results:

			Dynamic				Total
			.00	1.00	2.00	3.00	
Ultrasonography Findings		Count	0	1	0	3	4
		% of Total	.0%	2.0%	.0%	6.0%	8.0%
	Benign	Count	2	21	3	7	33
		% of Total	4.0%	42.0%	6.0%	14.0%	66.0%
	Malignant	Count	1	7	0	5	13
		% of Total	2.0%	14.0%	.0%	10.0%	26.0%
Total		Count	3	29	3	15	50
		% of Total	6.0%	58.0%	6.0%	30.0%	100.0%
Pearson Chi-Square6.678.Correlation is significant at p<0.005 Sig0.352							

4.4 Mammographic Results and Correlations:

Table (4.23): Cross Tabulation between the Mammographic Findings and Ultrasonography Doppler Blood Flow Results:

				Ultrasonography Doppler Blood Flow			Total
				few	free	more	
Mammography		**Count**	**2**	**2**	**4**	**0**	**8**
		% of Total	**4.0%**	**4.0%**	**8.0%**	**.0%**	**16.0%**
	Benign	**Count**	0	4	5	1	10
		% of Total	.0%	8.0%	10.0%	2.0%	20.0%
	Malignant	**Count**	3	7	18	3	31
		% of Total	6.0%	14.0%	36.0%	6.0%	62.0%
	Normal	**Count**	0	1	0	0	1
		% of Total	.0%	2.0%	.0%	.0%	2.0%
Total		**Count**	5	14	27	4	50
		% of Total	10.0%	28.0%	54.0%	8.0%	100.0%
Pearson Chi-Square7.187 Correlation is significant at p<0.005 Sig 0.618							

Table (4.24): Cross Tabulation between the Mammographic Findings and Lesion Shape at DWI:

			Lesion Shape at DWI		Total
			Irregular	Regular	
Mammography		**Count**	**4**	**4**	**8**
		% of Total	**8.0%**	**8.0%**	**16.0%**
	Benign	Count	5	5	10
		% of Total	10.0%	10.0%	20.0%
	Malignant	Count	13	18	31
		% of Total	26.0%	36.0%	62.0%
	Normal	Count	0	1	1
		% of Total	.0%	2.0%	2.0%
Total		Count	22	28	50
		% of Total	44.0%	56.0%	100.0%
Pearson Chi-Square1.102(a. Correlation is significant at p<0.005 Sig 0.777					

Table (4-25): Cross Tabulation between the Mammographic Findings and MRI Contrast Enhancement:

			MRI Contrast Enhancement			Total
			Intermediate	Slow	Strong	
Mammography		Count	3	2	3	8
		% of Total	6.0%	4.0%	6.0%	16.0%
	Benign	Count	3	3	4	10
		% of Total	6.0%	6.0%	8.0%	20.0%
	Malignant	Count	11	9	11	31
		% of Total	22.0%	18.0%	22.0%	62.0%
	Normal	Count	0	1	0	1
		% of Total	.0%	2.0%	.0%	2.0%
Total		Count	17	15	18	50
		% of Total	34.0%	30.0%	36.0%	100.0%
Pearson Chi-Square2.557. Correlation is significant at p<0.005 Sig 0.862						

Table (4-26): Cross Tabulation between the Mammographic Findings and BIRAD Results:

			BIRAD					Total
			.00	2.00	3.00	4.00	5.00	.00
Mammographic Finding		Count	**0**	**0**	**6**	**1**	**1**	**8**
		% of Total	**.0%**	**.0%**	**12.0%**	**2.0%**	**2.0%**	**16.0%**
	Benign	Count	0	1	6	2	1	10
		% of Total	.0%	2.0%	12.0%	4.0%	2.0%	20.0%
	Malignant	Count	1	0	24	3	3	31
		% of Total	2.0%	.0%	48.0%	6.0%	6.0%	62.0%
	Normal	Count	0	0	0	1	0	1
		% of Total	.0%	.0%	.0%	2.0%	.0%	2.0%
Total		Count	1	1	36	7	5	50
		% of Total	2.0%	2.0%	72.0%	14.0%	10.0%	100.0%
Pearson Chi-Square11.789 Correlation is significant at p<0.005 Sig 0 .463								

Table (4-27): Cross Tabulation between the Mammographic Findings and Dynamic Curve Results:

			Dynamic Curve Values				Total
			0.00	1.00	2.00	3.00	.00
Mammographic Finding		Count	0	6	0	2	8
		% of Total	.0%	12.0%	.0%	4.0%	16.0%
	Benign	Count	1	5	1	3	10
		% of Total	2.0%	10.0%	2.0%	6.0%	20.0%
	Malignant	Count	2	17	2	10	31
		% of Total	4.0%	34.0%	4.0%	20.0%	62.0%
	Normal	Count	0	1	0	0	1
		% of Total	.0%	2.0%	.0%	.0%	2.0%
Total		Count	3	29	3	15	50
		% of Total	6.0%	58.0%	6.0%	30.0%	100.0%
Pearson Chi-Square2.920. Correlation is significant at p<0.005 Sig 0.967							

Chapter Five

5.1 Discussion:

Accuracy can be written in terms of sensitivity, specificity and prevalence as:

Accuracy = Sensitivity × Prevalence + Specificity × (1 - prevalence).

Where prevalence is expressed as fraction, not as percentage.

Consider the following situation:

$$Accuracy = \frac{(Total\ \ number\ \ correct)}{(Total\ \ number\ \ of\ \ \ persons)}$$

As shown in table (4-1) statistical description of the sample age mean is 41.78, median is 39.50, Std. deviation is ±12.48, minimum is 26% and maximum is 80%.

As shown in table (4-2) classification of Sample according to age, frequency and percentages between 40 and 23 frequency 28 percentage 56% , between 55 and 41 frequency 15 percentage 30% , between 75 and 56 frequency 6 percentage 12% and plus 76 frequency 1 percentage 2%.

As shown in table (4-3) MRI diagnoses and classification of 50 breast lesions there are 34 benign lesions, 1 hematoma , 1 cyst , 1 degeneration, 13 fibroadenoma , 4 Fat Necrosis , 8 Fibrocystic Change, 2 myxoid fibroid , 3 papilloma and 1 pseudoangiomatous hyperplasia. Also there are 16 malignant 5 suspicious breast masses, 9 infiltrating ductal carcinoma, 1 intraductal papillary cancer and 1 popcorn calcification.

As shown in table (4-4) MRI diagnoses And classification of 50 breast lesions according to age classes are between 40 and 26 there are 21 benign lesions and 7 malignant lesions, between 55 and 41 there are 6 benign lesions and 9 malignant

lesions, between 75 and 56 there are 1 benign lesions and 5 malignant lesions and plus 76 there is only 1malignant lesions.P- Value =0.002 <0.05

In conventional breast MRI investigation, precontrast imaging was started either with T2 weighted images. Table (4-6) shows the characterization of lesions according to signal intensity .In the T2-weighted images water containing lesions or edematous lesions have an intense signal, and in this sequence cysts and myxoid fibroadenomas are very well identified. In most cases cancer as infiltrating ductal carcinoma, intraductal papillary cancer, popcorn calcification does not give up a high signal on T2 weighted images; therefore, these sequences can be useful in the differentiation between benign and malignant lesions, also most of these lesions can also be identified on T1weighted images, therefore previous studies suggested to use either T1 or T2 as they have the same value in that cases (Kelez, 2006; Kuhl et al., 1999). Signal intensity at diffusion-weighted imaging is inversely proportional to the degree of water molecule diffusion, that influenced by the histological structure .The motion of water molecules is more limited in tissues with a high cellular density as tumor tissue or with lipophilic cell membranes and less restricted in areas of low cellularity or where cell membranes have been damaged (Yoshikawa et al., 2007). The correlation between the MRI findings and the signal intensity is found to be significant at P value<0.05 in both T2 and DWI as 0.017and 0.000 respectively. The presence of isointense signal in DWI in the suspicious mass, degeneration, pseudoangiomatous hyperplasia and popcorn calcifications suggested that DWI may have lower sensitivity than DCE-MRI for detecting breast cancer. This was similar to what has been described previously by Yoshikawa et al. (2007). Therefore, and for more information, the study used the dynamic contrast enhanced MRI which uses curve type as it was recommended by the study done by Schnall et al.(2006). Hematomas containing intracellular components (oxyhemoglobin, deoxyhemoglobin, or methemoglobin) show

significantly reduced diffusion compared with hematomas containing lysed red blood cells (extracellular methemoglobin) (Fischbein et al., 2000).

Table (4-6) shows the signal intensities at diffusion-weighted imaging, T1 and T2 -weighted imaging for various pathologic conditions of the breast.

Dynamic Contrast Enhancement DCE-MRI scans were interpreted for each lesion and was assessed using the American College of Radiology (ACR) BI-RADS breast MRI lexicon (American College of Radiology, 2003) integrating morphologic and kinetic features, this was presented in table (4-7) .the correlation was found to besignificant between the MRI findings, Dynamic curves and BIRADS results as 0.032and 0.069 respectively at P value<0.05 Similar Findings were discussed by (Berg et al. 2004).

Who found that the BI-RADS MRI morphologic descriptors were not significantly predictive of the malignancy of lesions with non-mass like enhancement? Also Jansen et al. (2008), in an evaluation of the effectiveness of kinetic analysis of both masses and lesions with non-mass like enhancement, found that DCE-MRI kinetic information effectively differentiated benign from malignant mass lesions but was not useful in differentiating. The lesions are additionally described on the basis of their size, shape, margin and enhancement pattern. The kinetic curve evaluation includes a description of the contrast enhancement (20).

Lesion characteristics, including, shape regularity and irregularity were presented in table (4-8), 22(44.0%) of the lesions were found to be irregular and 28(56.0%) were found to be regular in its borders, the correlation between the diagnosis and the shape was found to be significant at P value <0.05=0.014 .And our results showed that the malignant lesions are greater in dimensions than the benign one .

DCE-MRI scans were interpreted, it shows 17 lesions have intermediate curve (16 were benign and 1was malignant), 15 lesions have slow curve (10were benign and 5were malignant), 18 lesions have strong curve (2were benign and 16was

malignant).The correlation between the MRI conventional diagnosis and contrast enhancement curves was found to be significant at P value =0.000.

This was presented in table (4-9) The Diffusion-weighted MRI (DWI) findings, DCE-MRI, BI-RADS, and dynamic curve assessment were recorded. This information was registered with detailed histopathology for each lesion. The consignation between histopathology results and MRI diagnosis, was found to be significant at P- Value <0.05 as 0.002.

DCE-MRI results were significantly correlated with histopathology results at P-Value <0.05 as 0.005, One Study revealed the specificity of DCE-MRI according to morphologic and kinetic criteria and reported to be between 37% and 97% (Orel and Schnall, 2001). The variable specificity of DCE-MRI is a limitation that can result in unnecessary biopsy (Elmore et al., 1998).

According to the definitions of American College of Radiology; masses categorized as BI-RADS 4 were considered to be suspicious for malignancy. Masses categorized as BI-RADS 5 were highly suggestive of malignancy. Masses were assigned BI-RADS category 3, is probably benign (Hiroko et al., 2011) Correlation between the histopathology and BIRADs results were found to be significant at p value <0.05 as 0.001 and 0.000 with the dynamic curve results. These were presented in tables (4-10), (4-14), (4-15), (4-16), and (4-17).

A review of studies about the MRI breast cancer, found a wide variation in the positive predictive value (PPV).Calculated as the percentage of lesions considered suspicious on MRI and found to be malignant on biopsy, PPV ranged from 24% to 89% (Elmore et al.,2005). Another study reported a PPV for MRI of 25% (Lehman et al., 2007), with 91 false-positive findings among 121 biopsies performed as a result of suspicious findings on MRI. Techniques to improve the specificity of breast MRI could reduce unnecessary biopsies and thus improve the overall accuracy of this highly sensitive tool for detecting breast cancer. When assess the

study findings, it shows that the diffusion-weighted breast imaging as a diagnostic imaging method can differentiate between the benign andmalignancy breast lesions without the use of contrast material. Ei Khouli et al (2010) showed an increase in diagnostic accuracy by adding diffusion-weighted imaging to conventional breast MR imaging ,similarly our results showed the highly significant correlations between the diagnosis of breast lesions and signal intensity changes in T2 weighted and DWI at P- Value =0.017 and 0.000 respectively. Therefore diffusion-weighted imaging findings cannot be assessed in isolation from findings obtained with other MR imaging sequences (T1 and T2-weighted imaging). Diffusion-weighted imaging has a low specificity for breast cancer and a low sensitivity (Woodhams et al., 2009) for the detection of infiltrating ductal carcinoma, and because the benign and malignant lesion signal intensity may be overlapped in different imaging sequences, therefore this combination method may improve the specificity of breast cancer assessment .However, the assessment of all these findings in combination indicates that diffusion-weighted imaging should be added to conventional and contrast-enhanced breast MR imaging as well as the diagnostic assessment by the curve types takes into account the increasing importance of detailed morphological and dynamic information. BIRADS gives acknowledged results when comparing with the histopathology findings and illustrates many of the morphological findings seen on contrast enhanced breast MRI. It also includes a lexicon that should be used for uniform reporting of the features seen on MRI (American College of Radiology, 2003).

5.2 Conclusions:

Appreciation of the significance of the additive diffusion weighted imaging, T1, T2 weighted MR imaging, Contrast enhancement MRI, Dynamic curves and BIRADS values for the assessment of breast lesions, will be useful in the analysis of breast MR images. It is likely that diffusion weighted breast imaging will be revealed to have an acknowledged task in breast MR imaging without the need of the invasive unnecessary biopsies.

5.3 Recommendations:

Fallow up for woman has family risk by MRI

MRI breast is the most evaluation of therapy respons in neoadjuvant chemotherapy

Unknown primary cancer when patients were diagnosed with metastasis and negative mammography and ultrasound, MRI breast should be strongly considered.

There are three important reasons to perform MRI breast after breast conserving therapy: an evaluation tool for detecting residual disease after positive tumor margins, evaluation when recurrence is suspected, and screening for patients that underwent breast conservative therapy in the past.

MRI breast can be an excellent modality to assess breast implant integrity.

5.4 References :

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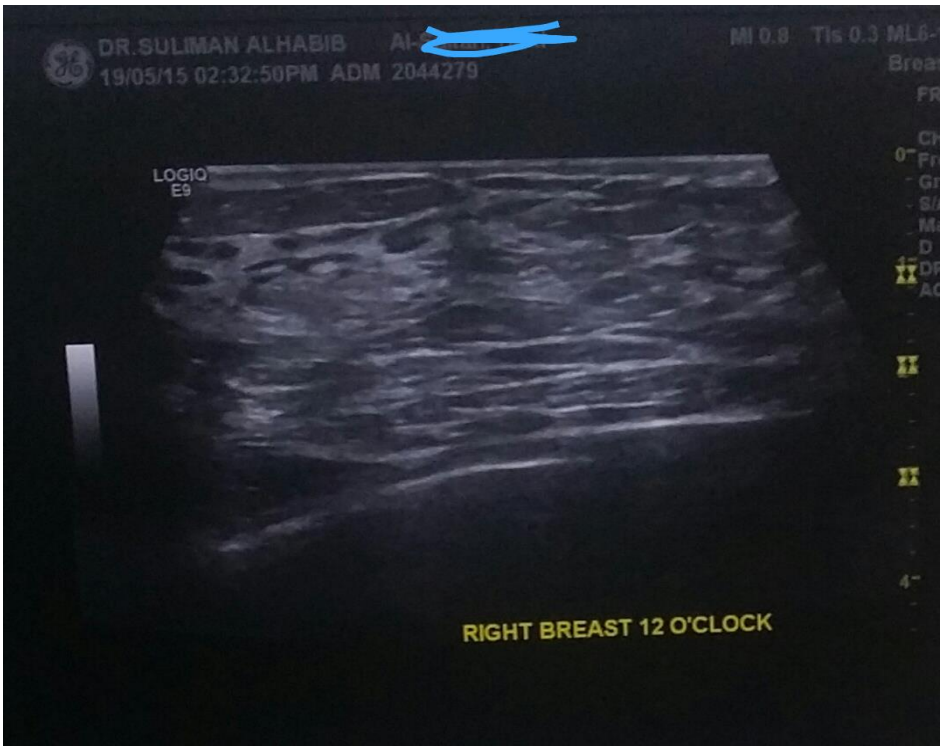
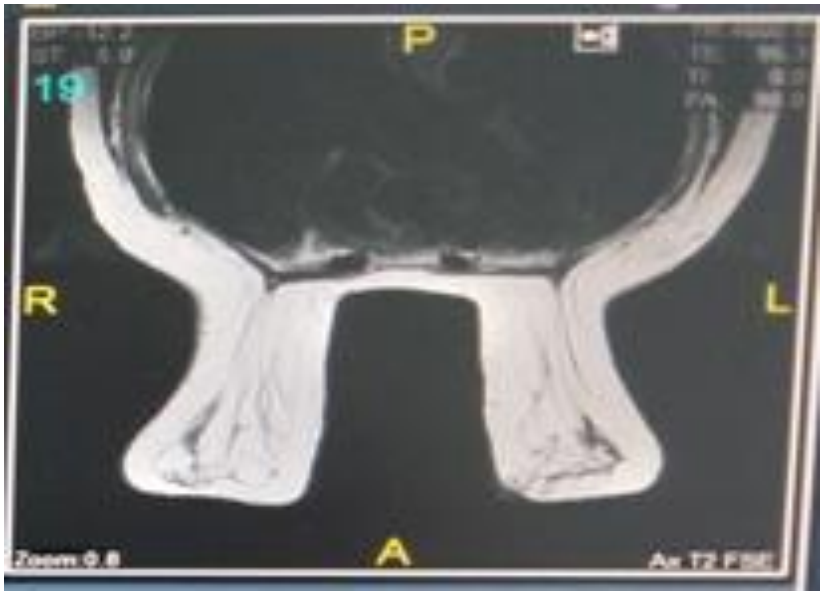
Appendix A

The Table of Data Collected during Study see page 106

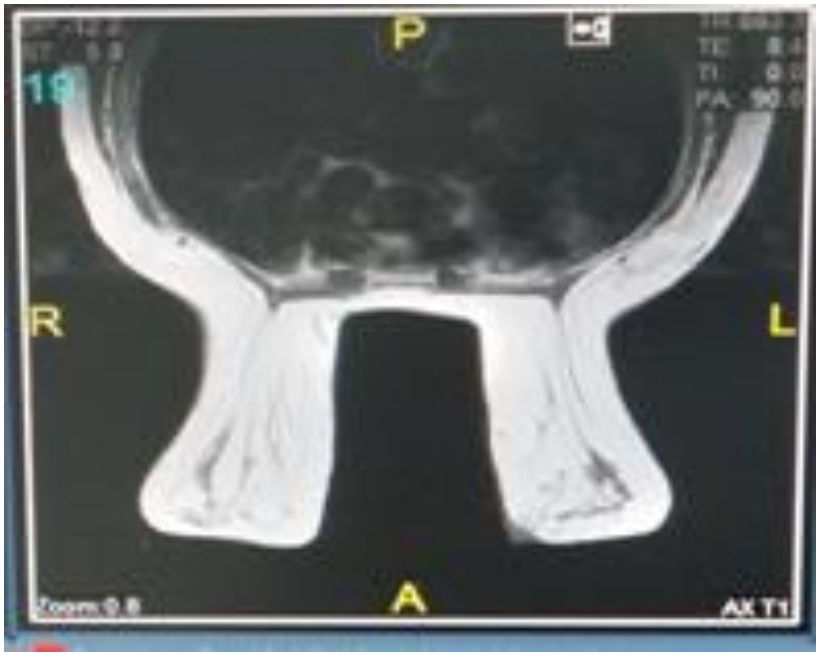
Appendix B



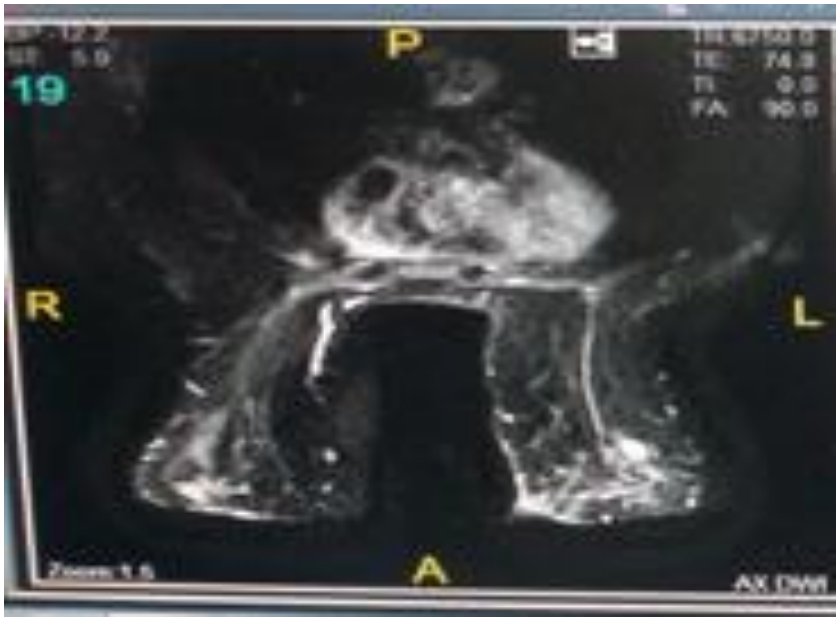
Normal ultrasound breast



T2 Fibroadenoma in left breast 2-3 o'clock



T1 Fibroadenoma in left breast 2-3 o'clock



DWI Fibroadenoma in left breast 2-3 o'clock