# INTRODUCTION

Breast cancer is the commonest cancer in women worldwide with an estimated 1.4 million cases in 2008.The rates have been increasing steadily and there is every indication that they will continue to do so over the next few decades **(Cuzick, 2010)**.

When patients present for diagnostic evaluations, the goal is to establish the correct diagnosis, accurately and efficiently. For some women this may include mammographic images only or additional ultrasound; for other patients additional mammographic views, an ultrasound, Magnetic Resonance image and a core biopsy are performed **(Gilda, 2007).**

Mammography is the main investigation for imaging of the breast cancer. Full field digital mammography is superior to standard mammography especially in the women with dense breasts but mammographic images are usually not enough to determine the existence of benign or malignant disease and the radiologist in some circumstances recommend further diagnostic studies **(Qaseem et al., 2007).**

Mammography is known to have high accuracy in detect breast cancer (sensitivity) but show high false positive rates (specificity) in the detection of breast malignancy (60-80%), resulting in unnecessary biopsies being performed **(Nelson, 2007).**

Magnetic resonance imaging (MRI) can discriminate benign from malignant lesions. Contrast enhanced MRI study of the breast is based on the enhancement pattern of the lesions and morphologic changes, with these two criteria breast MRI has a sensitivity of about 75-89 % in detecting malignant breast lesions, however there is an overlap of these criteria with benign lesions which leads to a reported specificity of about 50 to 90 % **(Marini et al., 2007).**

There is increasing number of published studies which mentioned that the specificity of the breast MRI could be increased by using diffusion –weighted imaging (DWI) **(Wenkel et al., 2007)**.

Diffusion-weighted magnetic resonance imaging (DW-MRI) depends on the microscopic mobility of water. This mobility, classically called Brownian motion, is due to thermal agitation and is highly influenced by the cellular environment of water. Thus, findings on DW-MRI could be an early harbinger of biologic abnormality **(Padhani et al., 2009).**

By using the DWI sequence, one can calculate the apparent diffusion coefficient (ADC), a quantitative measure that is directly proportional to the water diffusion. High cell proliferation in malignant tumors increases cellular density, creating more barriers to the extracellular water diffusion, reducing the ADC, and resulting in signal loss. This sequence appears to be a useful tool for tumor detection and characterization, as well as for monitoring and predicting treatment response **(Pereiera et al., 2009)**.

DWI is easy to obtain in short scan time and evaluate, and ADC values can differentiate between benign and malignant breast lesions with high sensitivity and specificity (**Tag-Aldeen &Abdulghaffar, 2013).**

# AIM OF THE WORK

To highlight the role of DW MRI in increasing the specificity of the MRI of the breast for detection of cancer breast in women with primary cancer or recurrent breast cancer.

# Part (I)

# GROSS ANATOMY OF THE BREAST

The breast or mammary gland is a modified sweat gland that has the specific function of milk production. An understanding of the basic anatomy is important in the interpretation of imaging studies and understanding to correlate radiologic-pathologic entities ***(De Paredes, 2007).***

The breast lies on the anterior and also partly the lateral chest wall over pectoralis major muscle and typically extends from the second to sixth rib in the vertical axis and from the sternal edge to the mid-axillary line in the horizontal axis. The breast tissue also projects into the axilla as the tail of Spence (the axillary tail). The breast extends laterally over serratus anterior muscle and inferiorly over the external oblique muscle and superior rectus sheath ***(Schnitt and Collins, 2009).***

The fascia forms septa called Cooper's ligaments, which attach the breast to the skin anteriorly and to the fascia of pectoralis posteriorly. They also run through the breast, providing a supportive framework between the two fascial layers ***(Ryan et al., 2004).***

The breasts are enclosed in thin skin that contains hair follicles, sebaceous and sweat glands called the superficial fascia. The superficial fascia of the breast covers the pectoralis, serratus anterior and external oblique muscles of the chest ***(Hussain et al., 2003).***

The deep membranous layer of the superficial fascia is separated from the fascia of the pectoralis major muscles and serratus anterior muscles by the retromammary or submammary space which contains superficial fascia that transvers the retromammary space **(Rosen, 2002)**.

Other identifying structures of the breast include the base, axillary tail and the inframammary crease which is the junction of the inferior portion of the breast with the anterior chest wall **(Fig.1)** ***(Hussain et al., 2003).***

The base of the breast is the posterior surface overlying the pectoralis muscle ***(Wentz and Hill, 1997).***

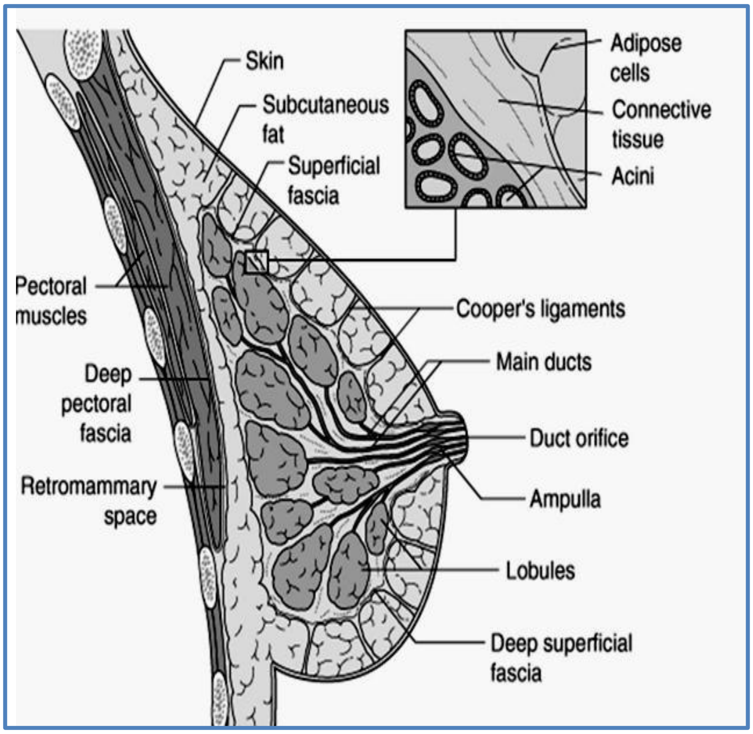


**Fig. (1):** Anatomy of the Breast ***(Quoted from Grainger, 2008)***

The nipple–areola complex is typically located over the fourth intercostal space in non pendulous breast ***(Sabel, 2009).***

The nipple is located in the center of the complex surrounded by the areola. Numerous sebaceous glands (the glands of Montgomery) and apocrine glands are present within the areolar dermis. The nipple dermis and subcutaneous tissue contain smooth muscle bundles arranged radially and longitudinally that serve to identify the nipple histologically. The nipple is rich in sensory nerve endings. Stratified squamous epithelium covers the nipple and areola. Lactiferous ducts course through the nipple dermis and open onto the epidermis ***(Moinfar, 2007).***

Centrally located on the surface of the breast is the areola – a circular pigmented area of skin 2-6 cm in size. Pigmentation of the areola is partially dependent upon estrogen levels. Elevations around the perimeter of areola are called the Morgani's tubercles. These tubercles are formed by the openings from the ducts of the Montgomery's glands. The Montgomery's glands secrete a fatty lubricant, which protects the nipple during lactation (nursing). In the center of the areola is the nipple protuberance, which contains 15-20 opening for the ducts that lead from the milk-producing lobes of the breast ***(Hussain et al., 2003).***

The nipple projects from the center of the breast anteriorly its shape varies from conical to flattened, depending on nervous, hormonal, developmental, and other factors**,** a normal nipple can be flattened or inverted. However, sudden inversion or flattening of the nipple may indicate underlying malignancy ***(Hussain et al., 2003).***

The breast is made up of three types of tissues: **fibrous, glandular** and **adipose**. The **fibrous** and **glandular** tissues are generally described as one tissue- fibroglandular. **Glandular** tissue is primarily located in the central portion of breast and in the extending upper outer quadrant toward the axilla, surrounded by fibrous and adipose tissues ***(Wentz and Hill, 1997).***

The **glandular tissue** is arranged in 15-20 lobes, with the fatty and fibrous tissue in between. The lobes are arranged like spokes of a wheel surrounding the nipple. Each lobe has a collecting duct called a lactiferous duct leading to the nipple ***(Wentz and Hill, 1997).***

The Cooper's ligaments separate individual breast lobes from each other. The Cooper's ligaments are visible on a mammogram as thin, gently curving lines, they can be foreshortened or straightened by fibrosis associated with breast cancer, causing skin retraction or localized architectural distortion ***(Wentz and Hill, 1997).***

The breasts can either be divided into quadrants or in relationship to the face of a clock for purposes of location of abnormalities. The four quadrants **(Fig. 2)** are the:

- **UIQ**: Upper Inner Quadrant
- **LIQ**: Lower Inner Quadrant
- **UOQ**: Upper Outer Quadrant
- **LOQ**: Lower Outer Quadrant

The exact locations within the quadrants can be represented by viewing each breast separately as a clock face ***(Peart and Hill, 2005)***

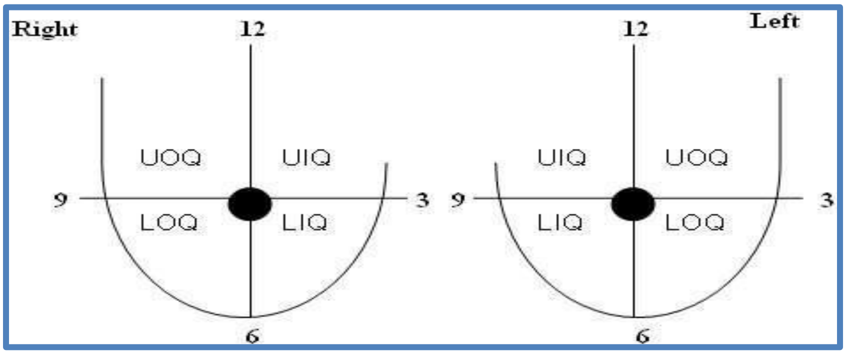


**Fig. (2):** Quadrant and clock divisions of the breast
***(Quoted from Peart and Hill, 2005).***

# The Axilla

## I. Boundaries:

The axilla is a pyramidal space located between the upper part of the thoracic wall and the arm. The axilla forms a passageway for the vessels and nerves from the neck to reach the upper limb. Anatomically, the axilla is taken to have an apex, a base and four walls, three of which formed by muscles ***(Macéa and Fregnani, 2006).***

- **Apex (or cervicoaxillary margin):** limited **medially** by the first rib, **posteriorly** by the upper margin of the scapula and **medial** face of the coracoid process of the scapula, and **anteriorly** by the clavicle.

- **Base:** This is an imaginary downward-turned surface that is wide at the thorax and narrow at the arm and correlates with the skin and thick layer of the fascia between, **anteriorly**, the **inferior** margins of the pectoralis major muscle (anterior axillary fold) and, **posteriorly**, the latissimus dorsi (posterior axillary fold).

- **Anterior wall:** This is formed by the pectoralis major and minor muscles.

- **Posterior wall:** This is formed by the subscapularis muscle in its upper part and the teres major and latissimus dorsi muscles, in its lower part.

- **Medial wall:** This is formed by the first four ribs with their intercostal muscles, and also the upper part of the serratus anterior muscle.

- **Lateral wall:** The anterior and posterior walls converge laterally towards the humerus, and the lateral wall is formed by the tendon of the long head of the biceps brachii muscle and, more medially, the coracobrachialis muscle ***(Macéa and Fregnani, 2006).***

**II. Contents of the axilla:** The contents of the axilla consist of the **axillary artery** and its branches, the **axillary vein** and its tributaries, **nerves** coming mostly from the brachial plexus, and finally **lymph vessels** and **axillary lymph nodes**. In its proximal portion, these elements are surrounded by the axillary sheath, which is a prolongation of the pre- vertebral portion of the fascia cervicalis. Between these elements, there is adipose tissue and mammary tissue that is cranially projected from the anterior face of the thorax into the axilla **(Fig. 3)** ***(Macéa and Fregnani, 2006).***

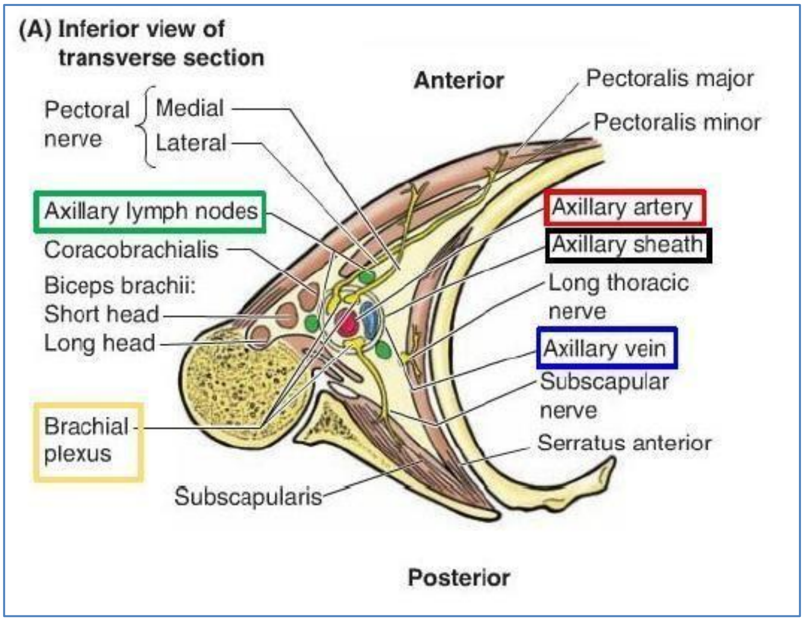


**Fig. (3):** Anatomy of the axilla ***(Quoted from Macéa and Fregnani, 2006).***

## Microscopic anatomy of the breast:

The breast is composed of 15 to 20 lobes or segments that converge at the nipple in a radial arrangement. The ducts from the lobes converge into 6 to 10 major collecting ducts that have openings at the nipple and connect to the outside. Each of these major ducts arborizes back from the nipple and forms a lobe or segment of glandular tissue that is supported by surrounding connective or stromal tissue**. *(Morris and Liberman, 2005).***

The distribution of lobes is not even as there is a preponderance of glandular tissue in the upper outer quadrant of the breast. Beneath the nipple openings, the lactiferous sinus is visible. The lactiferous sinus is a slight dilation of the ampullary portion of the major duct. ***(Morris and Liberman, 2005).***

The major ducts that converge below the nipple and drain each segment are 2mm in diameter. Each duct drains a lobe made up of 20 to 40 lobules. Each lobule contains 10 to 100 alveoli or acini. Each lobule also consists of branching ducts that divide into sub segmental structures and terminate in the terminal duct lobular unit ***(Morris and Liberman, 2005).***

The terminal duct lobular unit consists of the terminal duct and the acinus. The glandular tissue and ducts are surrounded by fat and supported by Cooper's ligaments, which are connective tissue elements that arise from stromal tissue and attach to the pre-pectoral fascia and dermis and support and suspend the breast tissue **(Figs.4 &5)** ***(Morris and Liberman, 2005).***

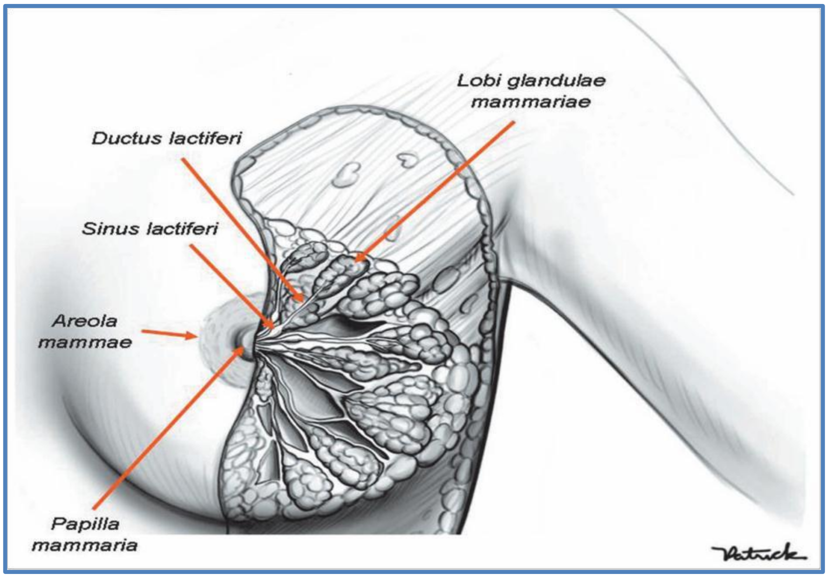


**Fig. (4):** Left breast diagram. The skin and subcutaneous layer have been extracted in order to view the lobi glandulae mammariae, ductus lactiferi and sinus lactiferi (anterior view) ***(Macéa and Fregnani, 2006).***

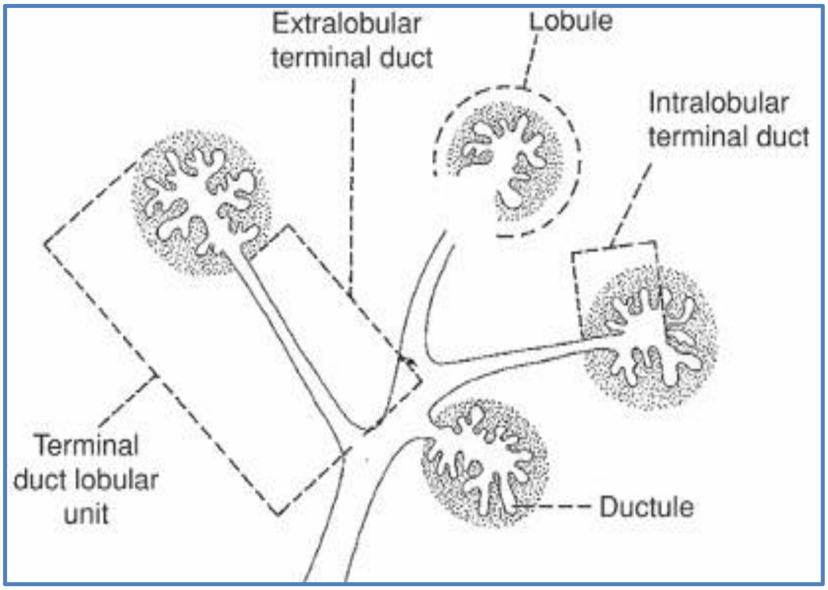


**Fig. (5):** Terminal Duct Lobular Unit ***(Quoted from De Paredes, 2007).***

**Effect of hormones:**

Increased or decreased glandularity of the breast is a part of the normal physiological changes that take place within the breast and may also vary with age, body weight and heredity. It can be related to hormonal fluctuations (whether normal or synthetic) including:

- Menstruation
- Pregnancy
- Lactation
- Menopause ***(Andolina and Lippincott, 2001)***

The female breasts are inactive during childhood because there are no lobules. The childhood breast will consist of small ducts within the fibrous tissue. Stimulation of breast growth is under the influence of the hormones produced in the ovaries. Estrogen causes elongation / branching of the ducts and increase in volume / elasticity of the connective tissue. Progesterone production in the ovaries occurs at ovulation forming the lobules ***(Andolina and Lippincott, 2001).***

The terminal duct lobular units (TDLUs) are referred to as acini in the lactating breast. Acini form only during pregnancy and reach full maturation during lactation. Lactation is influenced by progesterone and anterior pituitary hormones