INTRODUCTION

Early detection and diagnosis of malignant breast lesions are vital to survival. Although current imaging modalities such as mammography, ultrasonography, and magnetic resonance imaging focus on an anatomic approach, they do not provide sufficient data about the pathophysiology of malignant breast lesions. Positron emission mammography (PEM) is an innovative technology specifically designed to visualize the physiologic and metabolic processes in malignant breast lesions ***(Greene and George, 2012).***

Positron emission tomography is used as an adjunct imaging tool for the detection and staging of breast cancer and for assessing the response to treatment, but it is limited by its sensitivity in detection of small lesions Positron emission mammography uses a similar principle to that of positron emission tomography by using 18-F FDG to characterise malignant lesions, but has improved spatial resolution as the detectors are placed directly on the breast allowing compression. This also allows the benefit of direct correlation with mammograms and reconstructed three dimensional images ***(Kilburn-Toppin and Barter, 2012).***

PEM allows for detection of breast lesions as small as 2 mm and small foci of ductal carcinoma *in situ*. The results of a multicenter study examining the efficacy of PEM reported 91%

sensitivity and 93% specificity The reported limitations of PEM include a potential difficulty imaging breast lesions that are in a posterior location, the variable uptake of FDG in small and less metabolically active tumors, and false-positive findings from prior biopsy ***(Specht and Mankoff, 2012).***

The most probable role of PEM in clinical practice would be detection and characterization of primary breast lesions in preoperative surgical planning or prechemotherapy evaluation. PEM-guided biopsy is another potential role of PEM that also requires high imaging sensitivity ***(Eo et al., 2012).***

PEM and MR imaging had comparable breast-level sensitivity, although MR imaging had greater lesion-level sensitivity and more accurately depicted the need for mastectomy. PEM had greater specificity at the breast and lesion levels ***(Berg, 2010).***

AIM OF THE WORK

- Evaluation of the role of positron emission mammography in breast cancer imaging and management.
- To highlight the characteristics of performance of positron emission mammography.

ANATOMY OF THE FEMALE BREAST

The breast is a modified, differentiated apocrine sweat gland with a functional purpose of secreting milk during lactation. It is located in the superficial tissues of the anterior chest wall. The surface of the breast is dominated by the nipple and the surrounding areola ***(Glenn, 2001).***

The mature breast has an eccentric configuration, with the long axis diagonally placed on the chest wall largely over the pectoralis major muscle and extending into the axilla. The peripheral anatomic boundaries of the breast are not precisely defined, except at the deep surface where the gland overlies the pectoralis fascia. Superficially, the breast extends over portions of the serratus anterior muscle, laterally, inferiorly over the external oblique muscle and superior rectus sheath, and medially to sternum ***(Rosen, 2001).***

The protuberant part of the human breast is generally described as overlying the second to the sixth ribs, and extending from the lateral border of the sternum to the anterior axillary line. Actually, a thin layer of mammary tissue extends considerably farther from the clavicle above to the seventh or eighth ribs below, and from the midline to the edge of latissimus dorsi muscle posteriorly ***(Russell et al., 2000).***

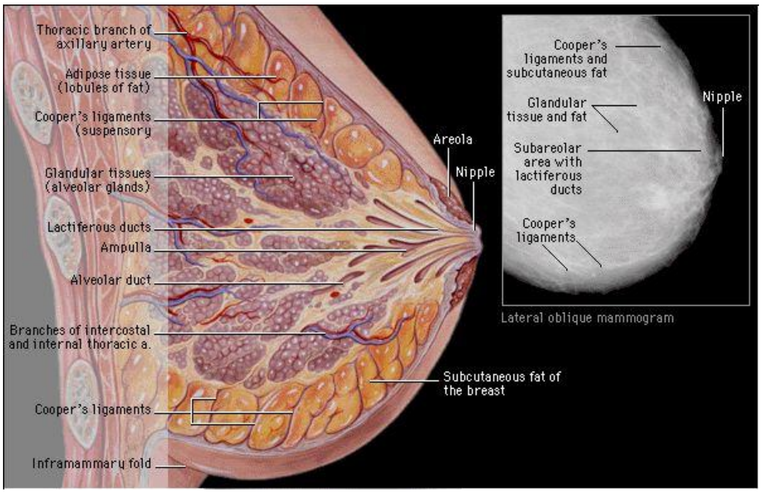

Fig. (1): Anatomy of the breast ***(Moore et al., 1999).***

The axillary tail

The axillary tail of the breast (tail of Spence) is a breast extension towards the lateral margin of the chest and into the axilla. It has a duct, which drains into the ductal system of the major gland. In some normal cases it is palpable, and in a few it can be seen premenstrually or during lactation. A well-developed axillary tail is sometimes mistaken for a mass of enlarged lymph nodes or a lipoma ***(Hendriks et al., 2002).***

The internal structure of the mammary gland

The normal adult female breast *(Fig.1)* is composed of an admixture of epithelial and stromal elements with variable adipose tissue typically present in the interlobular stroma, and not amongst the lobules. The epithelial elements are glandular tissue or tubulo-alveolar type consisting or a series or branching ducts which connects the structural and functional units of the breast, the lobules, to the nipple. The stroma is composed of variable amounts of adipose tissue and fibrous tissue, and comprises the majority of the breast volume in the non lactational state.The relative abundance of parenchyma and stroma varies according to age, parity and other factors ***(Hayes, 2000).***

The mammary gland (mamma = breast) consists of 15-20 lobes or segments, separated by adipose tissue. The amount of adipose tissue, not the amount of milk produced, determines the size of the breast ***(Hendriks et al., 2002)***.

Each lobe is drained by one lactiferous duct (lact = milk, ferre = to carry). Lactiferous ducts run dorsally in the long axis of the nipple, enveloped in an areolar cuff, and then spread radially. Two or three lactiferous ducts unite to form a total of five to eight lactiferous sinuses, which exit at the nipple ***(Hendriks et al., 2002)***.

The lobule is the basic structural unit of the mammary gland. Each lobe contains hundreds of lobules, composed of grape like clusters of milk-secreting glands termed alveoli (alveolus= small cavity) embedded in connective tissue. Surrounding the alveoli are spindle shaped cells called myoepithelial cells, whose contraction helps to propel milk toward the nipple ***(Hendriks et al., 2002)***.

Terminal ductal lobular unit (TDLU) is the basic histological unit. It consists of the extra- and intralobular terminal ducts and the blind ending acinar ductules. The lobule consists of 25-35 acini. The acini are (milk producing) the glandular component of the breast lobules ***(Hendriks et al., 2002).***

The ligaments of Cooper

Anatomically, the breast lies in a space within the superficial fascia. Superiorly this layer is continuous with cervical fascia and inferiorly with the superficial abdominal fascia of Cooper. Fibrous strands extend from the dermis into the breast, forming the suspensory ligaments of Cooper, which attach the skin and nipple to the breast. Cooper's ligaments are more extensive in the upper part of the breast. Cooper's ligaments are hollow conical projections of fibrous tissue filled with breast tissue, the apices of the cones being attached firmly to the superficial fascia and thereby to the skin overlying the breast. They are considered to be the fibrous "skeleton" supporting the breast glandular tissue. Distortion or contraction of the suspensory ligaments by parenchymal lesions may be manifested by skin dimpling or nipple retraction ***(Rosen, 2001).***

Two-thirds of the breast rests on the deep membranous layer of the superficial fascia of the pectoral fascia overlying the pectoralis major, the other 3^{rd} rests on the fascia covering the serratus anterior muscle. Between the breast and these fasciae is a potential space, the retro-mammary or sub-mammary space (bursa), which contains a loose adipose and connective tissue allowing the breast some degree of movement on the pectoral fascia. Extensions of the membranous superficial fascia that traverse the retro-mammary space act as posterior suspensory ligaments. Neoplastic or inflammatory infiltration of the retro mammary space is associated clinically with fixation of the breast to the chest wall ***(Rosen, 2001).***

The nipple

The nipple is covered by thick skin (stratified squamous epithelium) with corrugations. It is un-pigmented in the pre-pubertal breast. Melanin pigmentation develops after menarche, increasing during pregnancy, and persists to a variable degree thereafter. Near its apex lie the orifices of the lactiferous ducts. The nipple contains smooth muscle fibres arranged concentrically and longitudinally, thus it is an erectile structure which points outwards. Sebaceous glands are present in the skin of the nipple ***(Rosen, 2001).***

The areola

The areola (a-RE-O-La, areola = small space) is a ring of skin surrounding the breast nipple that undergoes pigmentary changes similar to the nipple. It contains involuntary muscles arranged in concentric rings as well as radially in the subcutaneous tissue. The areolar epithelium contains numerous sweat glands and sebaceous glands, the latter of which enlarge during pregnancy and serve to lubricate the nipple during lactation (Montgomery's glands).These glands atrophy after menopause. The glands of Montgomery are modified sebaceous glands that open on the surface of the areola via the tubercles of Morgagni. The latter structures are visible, especially during pregnancy, around the base of the nipple ***(Rosen, 2001).***

The axilla

The anatomic boundaries of the axilla are visible externally when the arm is raised. It is bounded superiorly by the lower border of the pectoralis major muscle, which passes laterally to the humerous from the chest wall and tapers toward its site of insertion, below it is the pectoralis minor muscle. With the arm raised to the horizontal, the axillary artery runs below and parallel to the pectoralis minor muscle and inferior to that vessel is the larger-caliber axillary vein. The thoracodorsal neurovascular bundle descends on parasagittal plane at right angle to the axillary vessels. Most of lymph nodes in this region are embedded in the axillary lymphatic tissue and fat ***(Madjar, 2000).***

The axillary fascia at the dome of the pyramidal axillary space is formed by an extension of pectoralis major muscle. A fascial layer arising from the lower border of the pectoralis minor joins an extension of the pectoralis major fascia to form the suspensory ligament of the axilla in continuity with the fascia of the latissimus dorsi muscle. An inconstant muscle band in this fascial plane is referred to as the suspensory muscle of the axilla. The fascial boundaries of the axilla provide important landmarks for the en bloc dissection of the axillary contents ***(Rosen, 2001).***

Breast quadrants

The breast is often divided into four quadrants based on horizontal and vertical lines crossing at the nipple. An axillary tail of breast tissue, sometimes termed the “tail of Spence,” extends laterally across the anterior axillary fold. Alternatively, findings can be localized as the time on the face of a clock (e.g., 3 o'clock) and the distance in centimeters from the nipple ***(Bickley and Szilagyi, 2009).***

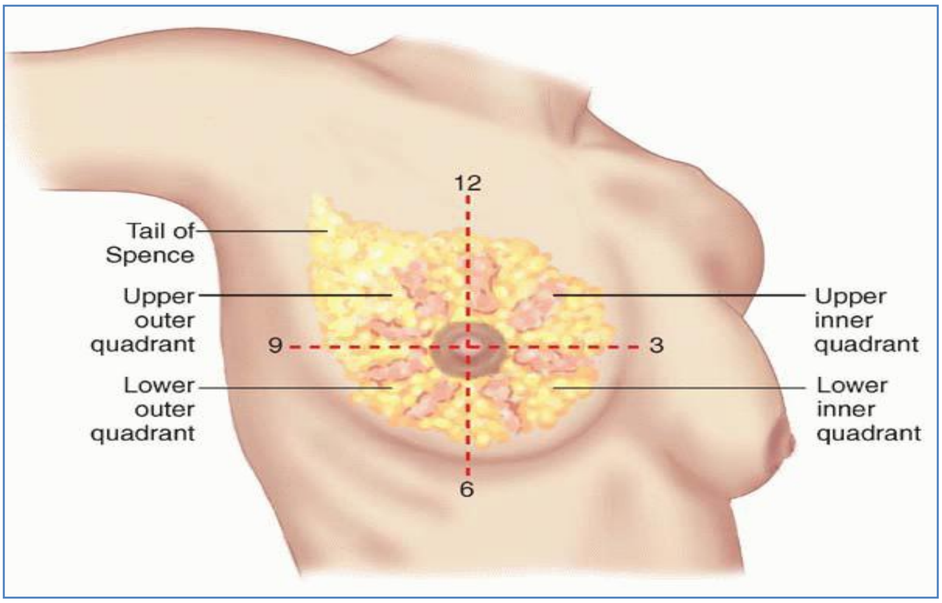

Fig. (2): Breast quadrants.

Microscopic Anatomy

The normal microscopic anatomy of the lobules *(Fig.3)* is not constant, because the structure and histologic appearance of the lobule in the mature breast are subject to changes associated with the menstrual cycle, pregnancy, lactation, exogenous hormone administration, and menopause ***(Christovet al., 1991).***

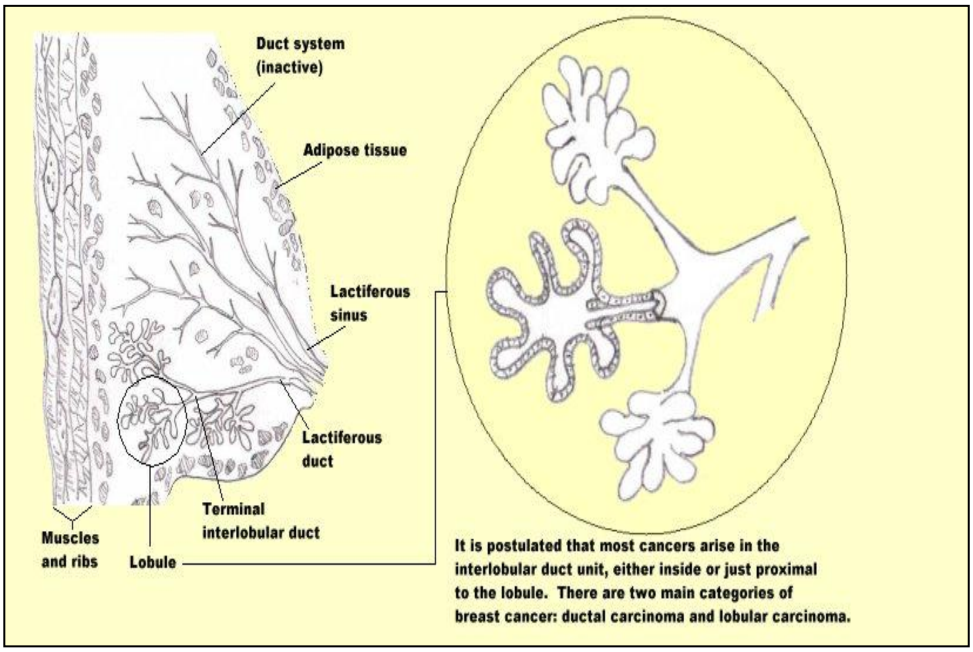

Fig. (3): Microscopic anatomy of female breast sagittal section and histology of the glandular unit ***(Ryan, 2000).***

Furthermore, there is variation in the functional state of individual lobules regardless of physiologic circumstances, an observation that suggests that individual lobules or lobules in the regions of the breast have intrinsic differences in response to hormonal stimuli ***(Christovet al., 1991).***

Each of the major lactiferous ducts terminates in and exits from the breast at the nipple via a secretory pore forming the lactiferous duct orifice. The superficial portion of the duct orifice is lined by squamous cells where the duct traverses the epidermis, and the squamous epithelium may extend for a short distance into the most terminal portion of the lactiferous duct. The squamo-columnar junction, where the squamous epithelium joins the glandular duct epithelium, normally it is distal to a dilated segment of the lactiferous duct, referred to as the lactiferous sinus ***(Pechoux et al., 1999).***

The lactiferous ducts in the nipple are surrounded by circular and longitudinal arrays of smooth muscle fibres embedded in fibrocollagenous stroma. Some of these muscle fibres attach to the skin of the nipple and areola. Sebaceous glands associated with the overlying skin protrude downward into the superficial stroma of the nipple. The lactiferous ducts extend into the breast through a series of branches that diminish in caliber from the nipple to the terminal ductal-lobular units, which are embedded in specialized, hormonally responsive stroma. Extra-lobular ducts are lined by columnar epithelium that is supported by myoepithelial cells, a basement membrane, and surrounding elastic fibres ***(Pechoux et al., 1999).***

In addition to the elastic fibres, the normal periductal stroma contains a space scattering of lymphocytes, plasma cells, mast cells, and histocytes. Ochrocytes are periductal histiocytes with cytoplasmic accumulation of lipofuscin pigment. These pigmented cells become more numerous in the postmenopausal breast and in association with inflammatory or proliferative conditions ***(Davies, 1994).***

The histological appearance of the ducts and glands of Montgomery in the subareolar tissues resmbles the major lactiferous ducts of the nipple, except the contour tends to be smoother. Serial secretions have demonstrated direct connections between lactiferous ducts draining lobular parenchyma and the ducts of Montgomery's glands in the tubercle of Morgagni ***(Schnitt et al., 1993).***

Mammary secretion occurs in the lobules, which consist of groups of alveolar glands encompassed by specialized stroma. Alveoli are connected by intralobular ductules combined to form single terminal lobular duct that drains into the extralobular duct system. In lobules, alveolar glands are formed along and at the end of intralobular ductules. In histologic sections, these glandular structures appear as blunt or round saccules protruding from the duct lumen ***(Rosen, 2001).***

The resting lobular gland is lined by a single layer of cuboidal epithelial cells supported by underlying, loosely connected myoepithelial cells. The intralobular stroma contains more capillaries and is less densely collagenized than the interlobular stroma ***(Rosen, 2001).***

Cuboidal epithelial cells line the ducts. Myoepitheliocytes form a discontinuous layer between lining cuboid cells and basement membrane. The myoepitheliocytes transport the milk through the ducts. The basement membrane separates the epithelial cells from the connective tissue. Evaluation of the basement membrane is important because its interruption by malignant cells mean that the carcinoma is invasive ***(Hendriks, et al, 2002).***

Breast development:

Prenatal development

The epithelial mammary bud appearing at a gestational age of 35 days; by day 37 this has become a mammary line extending from the axilla through to the inguinal region. Usually invagination of the thoracic mammary bud into the mesenchyme occurs by day 49, with involution of the remaining mammary line. Nipple formation begins at 56 day and primitive ducts (mammary sprouts) develop at 84 days with canalization occurring at about the 150th day ***(Peter et al., 1995).***

Postnatal development:

In the neonate there are lactiferous ducts but no alveoli. After puberty, lobule formation occurs (exclusively in females), when there is branching of ducts and development of lobules from terminal ducts, stimulated by ovarian oestrogens, they develop branches whose ends form solid, spheroidal masses of granular polyhedral cells, which are potential alveoli ***(Peter et al.,1995).***

During the menstrual cycle:

In the follicular phase the stroma becomes less dense and various changes take place in the ducts, including the expansion of their lumen, with occasional mitoses but no secretion. In the luteal phase, there is a progressive increase in stromal density; the ducts have an open lumen containing secretion, with flattening of the epithelial cells, cell proliferation reach maximal on day 26. Thereafter, the ductal system undergoes reduction, with epithelial cell apoptosis greatest on day 28 of the cycle ***(Peter et al., 1995)*.**

In pregnancy and during suckling:

As the output of placental oestrogen and progesterone rises during pregnancy, the ducts increase in the number and length of their branches; the secretory alveoli proliferate, with the synthesis and secretion of milk the alveoli expand as their lumen becomes filled. In the stroma there is a concomitant reduction in adipose tissue, but the number of the lymphocytes increase; blood flow through the breast also increases ***(Peter et al., 1995)*.**

Post lactation changes:

When lactation cease the secretory tissue undergoes some involution, but the ducts and alveoli never return completely to the pre-pregnant state. Two major processes are responsible for the regression of the alveolar-ductal system, a reduction in