INTRODUCTION

Breast cancer is the most common malignant disease in Western women. In these patients, it is not the primary tumor, but its metastases at distant sites that are the main cause of death ***(Forman D, et al., 2010).***

Risk factors of breast cancer may be divided into preventable and non preventable. Breast cancer, like other forms of cancer, can result from multiple environmental and hereditary risk factors. The term **environmental**, as used by cancer researchers, means any risk factor that is not genetically inherited (***Ward E, et al.,.2011).***

Metastatic breast cancer is considered an incurable disease. Survival of patient with metastatic breast cancer is between 2- 3 years and majority of them do not survive beyond 5 years (***Bray F, et al., 2013).***

Recently, the rates of metastasis and mortality in breast cancer patients have decreased as a result of early diagnosis by sono mammographic screening and the implementation of systemic Adjuvant therapy. Adjuvant therapy can help to eradicate breast tumor cells that might have already spread to distant sites by the time of diagnosis (***Ward E, et al., 2011).***

The surgery of breast tumors with distant metastases is indicated only to prevent local complications. It is generally accepted that local therapy provides no survival advantage once metastases have occurred and that, in fact, tumor excision may further stimulate the growth of the metastases ***(Ferlay J, et al., 2013).***

AIM OF THE WORK

Is to compare between the role surgical resection of primary breast tumor in female with metastatic breast cancer with non surgical management as regard size of metastatic tumor, tumor markers and survival rate.

ANATOMY OF THE BREAST

Female breast

Female breast is formed mainly of mammary glands and fat. The mammary glands are modified sweat glands in structure and function and whose site of origin determines certain morphological features. Their modified structure differs from that of either merocrine or apocrine type of sweat glands. Their modified function is to provide the newborn infant with specialized nutrients. Their superficial origin accounts for the absence of a true fibrous capsule or sheath surrounding the glands. The glands do not benefit from a specialized vascular supply or innervation, as all these needs are derived from existing structures serving the thoracic wall (***Lawson L, et al., 2010)***.

Anatomy of the Breast

The breast forms a secondary sexual feature of the female and is the source of nutrition for the neonate. They are also present in a rudimentary form in males. At birth the mammary glands are alike in their stage of development in both sexes; the combination of fetal prolactin and maternal oestrogen may give rise to transient hyperplasia and secretion of 'witch's milk'. In males, thereafter, the mammary glands normally remain

undeveloped; in females at puberty, in late pregnancy and during the period of lactation they undergo further, hormone-dependent and developmental changes (***Standring S, et al., 2010)***.

Breast shape and size depend upon age, genetic, racial, dietary factors, parity and menopausal status of the individual female. Breasts may be hemispherical, conical, piriform, variably pendulous or thin and flattened. The size of the adult female breast varies widely among individuals and considerable discrepancy in breast size is seen between the breasts of an individual women. This is a rarely a sign of breast disease (***Morrow M, et al., 2011).***

In young adult female, each breast is a rounded eminence lying within the superficial fascia, largely anterior to the upper thorax but spreading laterally to a variable extent (Fig. 1). It lies between the second and sixth ribs, from the sternal edge medially almost to the midaxillary line laterally in the transverse plane. The superolateral quadrant of the breast tissue frequently extends towards the axilla as the axillary tail of Spence. The breast lies upon the fascia of pectoralis major muscle superiorly; inferolaterally it is bounded by the fascia of the serratus anterior and inferiorly external oblique and its aponeurosis. Between the breast and the deep fascia is a loose connective tissue in the "submammary space". This allows the breast some degree of movement on the deep pectoral fascia. Bands of the fibrous

tissue, known as Cooper's ligaments, extend from the fascia to the fibrous tissue of the dermis and support the breast. The breast is composed of skin, subcutaneous tissue, breast tissue and nipple and areola. Fig (2) ***(Morrow M, et al., 2011).***

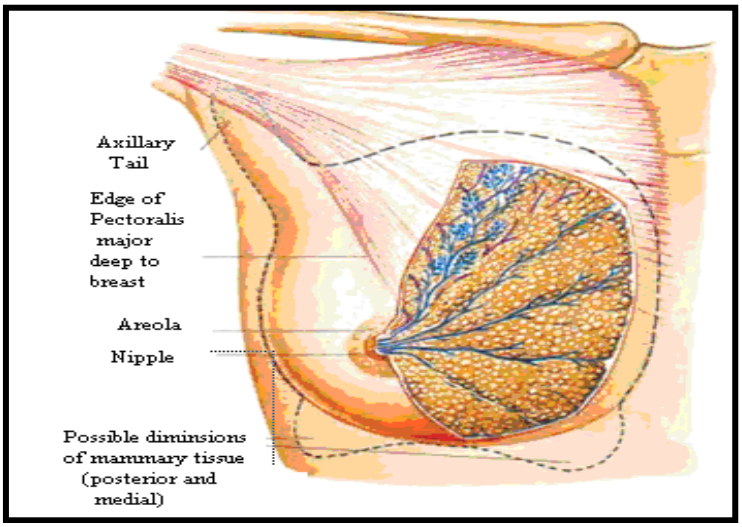


Fig. (1): The macroscopic and microscopic structure of the female breast.

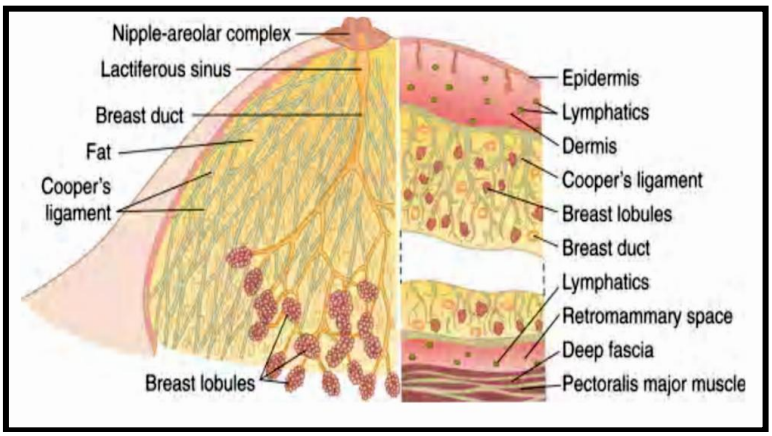


Figure (2): Cut-away diagram of a mature resting breast ***(Morrow, et al., 2011).***

Skin

The breast is covered by a typical thin skin of the anterior thoracic wall bearing fine hair. The skin of the nipple and the surrounding areola is modified and lacks hair. Here, the skin has a convoluted surface and contains many sweat and sebaceous glands which opens directly on to the skin surface. The oily secretion of the sebaceous glands is a protective lubricant during lactation. Montgomery glands are located at the periphery of the areola and their openings form nodular elevations known as tubercles of Morgagni. These glands are capable of secreting milk and represent an intermediate structure between sweat and mammary glands. Melanocytes are quite numerous in the skin of the nipple and areola, giving them a darker colour than the remainder of the breast. Further darkening of the nipple and areola occurs during the second month of pregnancy, a change that persists to a variable degree. The nipple, areola regions and the reminder of the breast are richly supplied with sensory innervation ***(Gabriel A, et al., 2009).***

The Nipple and Areola

The nipple projects from the centre of the breast anteriorly (Fig 3); its shape varies from conical to flattened, depending on nervous, hormonal, developmental and other factors. Its level in

the thorax varies widely; but is at the fourth intercostal space in most young women. In the nulliparous it is pink; light brown or darker in colour, depending on the general melanization of the body. Occasionally the nipple may not evert during prenatal development and it remains permanently retracted and so causes difficulty in suckling. The nipple is covered with keratinized stratified squamous epithelium. Its stroma contains dense connective tissue, with smooth muscle surrounding the lactiferous ducts ***(Maxwell GP, et al., 2009).***

The areola is a disc of skin, which circles the base of the nipple. Its colour varies from pink to dark brown depending on parity and race. The areola contains the large areolar glands of Montgomery which can be seen by the naked eye and become more prominent during pregnancy. The function of the Montgomery glands is to produce a lubricant that bathes the nipple and areola tissue during lactation. Occasionally Montgomery glands can become obstructed and develop a localized infectious process. Beneath the nipple and areola is the erector areola muscle: bundles of smooth muscle fibers arranged circumferentially and radially that produce erection of the nipple when stimulated ***(Graham S, et al., 2010).***

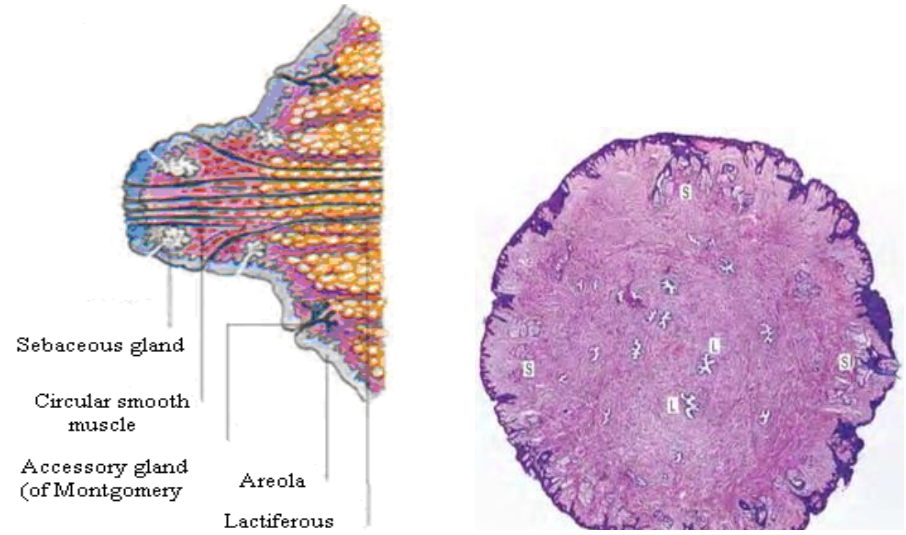


Figure (3): (A) Section of the nipple (B) Cross-section of the nipple. There is a corrugated layer of stratified squamous keratinized epithelium over the nipple surface; 20 or more lactiferous ducts (L) open onto the surface; sebaceous glands (S) are deep to the epidermis ***(Maxwell GP, et al., 2009).***

Axilla:

The axilla is pyramidal in shape with its base inferiorly (the axillary floor) and the apex superiorly (costoclavicular angle) (I)Anterior wall is formed by the posterior border of pectoralis major muscle at the surface and by the subclavius and pectoralis minor muscles in depth. The pectoralis minor muscle artificially divides the axilla into three parts: sub pectoral, retro pectoral and supra pectoral which corresponds to the classic "Berg's levels". These levels are not anatomically real, but the simplicity of the description made by this pathologist, more than 50 years ago, made it acceptable by the international community

;(II). Medial wall is formed by the thoracic wall which is made of the first five ribs covered by the serratus anterior, (III) Posterior wall is formed by the subscapularis and the latissimus dorsi, (IV) Laterally by the anterior border of the latissimus dorsi, (V) Superiorly by the axillary vein, (VI) Infront and lower part by the clavi-pectoro-axillary fascia, key for opening the axillary pit during lymph node dissection. In the axilla there are vascular and nervous elements: (a) The nerve to serratus anterior muscle (or Charles bell nerve) which goes down along the muscle and represents the internal boundary for the dissection; (b) The $1^{s'}$, 2^{nd} and 3^{ld} intercostal perforator nerves (or inter-costal brachial nerves) which cross the thoracic wall and the axilla horizontally to supply the integument of the internal aspect of the axilla and the arm. There is an anastomosis between the 2^{nd} perforator and the internal brachio cutaneous accessory nerve; (c) the nerve to latissimus dorsi which runs vertically along the subscapularis muscle. The sub scapular artery accompanies that nerve. This artery divides to give a scapular branch (circumflex artery) and a thoracic branch (thoraco dorsal artery). This thoracic branch divides later into an anterior branch for the serratus anterior, an external branch for the latissimus dorsi and an inferior branch descending towards the thoracic wall. This latter, constitutes the inferior boundary for dissection. The thoracic branch, accompanied with its vein, together with the nerve to latissimus dorsi muscle, constitutes the vasculo

nervous pedicle of the latissimus dorsi; (d) the axillary vein under the artery constitute the superior limit of the dissection. The axillary artery above the vein should not be seen during the axillary lymph node dissection (***Woods WC, et al., 2010)***.

Cutaneous Vascular Supply and Lymphatic Drainage:

Medially, the skin of the breast is supplied by branches from the anterior intercostal arteries. Laterally, the skin is supplied by branches from the lateral thoracic artery (a branch of the axillary artery) and by the lateral cutaneous branches of the posterior intercostals arteries. The venous drainage of the areola and the surrounding skin is into a circular venous plexus, which drains into the veins, which accompany the corresponding arteries, i.e. the axillary, internal thoracic and intercostals veins. The density of the lymphatic draining channels in the skin of the breast is much greater than that for the soft tissue of the breast. Lymph drainage is towards the axilla. The lymphatics of the lateral skin of the breast including the subareolar plexus pass to the pectoral nodes. Vessels near the sternal edge pass between the costal cartilages to parasternal nodes and also anastomose across the sternum. A few vessels from the upper pectoral region ascend over the clavicle to drain to the inferior deep cervical nodes ***(Maxwell GP, et al., 2009).***

Soft tissue

The breast tissue includes both epithelial parenchymal elements and stroma. The epithelial internal (glandular) structure of the breast compresses about 10% to 15% of the breast mass, with the remainder being stroma. Each breast consists of 15 to 20 lobes of glandular tissue that are supported by a framework of fibrous connective tissue. Within each lobe, the lobules are composed of branched tubuloalveolar glands. Each lobule ends in a lactiferous duct. These ducts dilate into lactiferous sinuses beneath the nipple. The space between lobes is filled with adipose tissue. Variations in the breast size are accounted for by differences in the amount of adipose tissue in the breast rather than epithelial elements. Much of the epithelial tissue of the breast is found in the upper outer quadrant, which is why this is the most frequent site of both benign and malignant breast disease ***(Gabriel A, et al., 2009).***

The lobes of the breast are subdivided into lobules which are made up of branched tubuloalveolar glands. Each lobe ends in a lactiferous duct 2 to 4mm in diameter. Beneath the areola the lactiferous ducts dilate into lactiferous sinuses and the open through a constricted orifice onto the nipple (Fig 4). Beneath the nipple and areola are bundles of radially arranged smooth muscle fibers that are responsible for the erection of nipple in response to a variety of stimuli (***Jones GE, et al., 2010).***

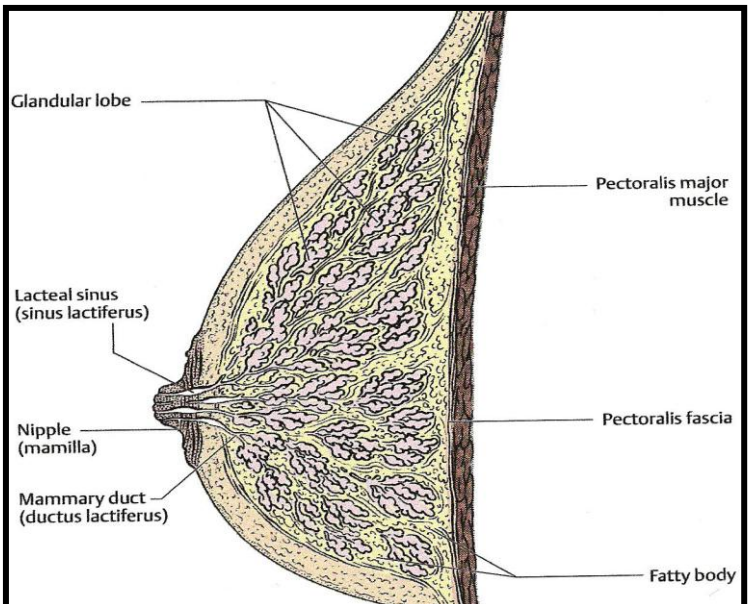
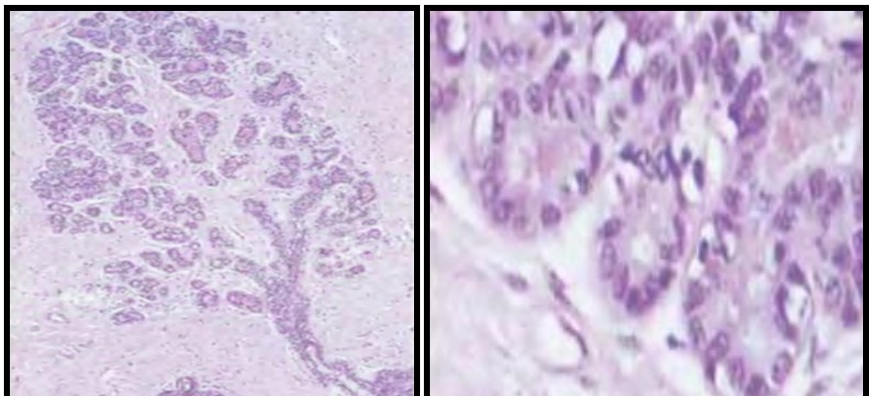


Figure (4): Female breast ***(Jones GE, et al., 2010).***

Microstructure

The microstructure of breast tissue varies with age, time in the menstrual cycle, pregnancy and lactation. The following description relates to the mature resting breast. For most of their lengths, the ducts are lined by columnar epithelium (Fig 5). In the larger ducts these are two cells thick, but in smaller ones only a single layer of columnar or cuboidal cells is present. The bases of these cells are in close contact with numerous myoepithelial cells of ectodermal origin (Fig 6). Myoepithelial cells are so numerous that they form a distinct layer surrounding the ducts and presumptive alveoli and give the epithelium a bilayered appearance ***(Thorne CH, et al., 2007).***

Lactiferous ducts draining each lobe of the breast pass through the nipple and open on to its tip as 15-20 orifices. Each of these ducts is slightly expanded near its orifice as a lactiferous sinus, which, in the lactating breast, is further dilated by the presence of milk (Fig 7). Each lactiferous duct is therefore connected to a system of lobules, surrounded by connective tissue stroma, collectively forming a lobe of the mammary gland. Lobules consist of the portions of the glands that have secretory portion. Their structure varies according to hormonal status. In the mature resting breast each lobule consists of a cluster of blind-ended, branched ductules whose termini lack terminal alveoli (acini), which are the sites of milk secretion in the lactating breast. The stratified cuboidal lining is replaced by keratinized stratified squamous epithelium, continuous with the epidermis, close to the openings of the lactiferous ducts on the nipple (***Beasley RW, et al., 2007).***



A **B**

Fig. (5): (A) glandular lobule surrounded by collagenous interlobular connective tissue in the mature resting breast (**B)** A terminal duct (bottom right) branches extensively to terminate in rudimentary acini, which are shown at higher magnification in the lower panel ***(Thorne CH, et al., 2007).***

Internally the nipple is composed mostly of collagenous dense connective tissue and contains numerous elastic fibers which wrinkle the overlying skin. Smooth muscle cells are arranged in a predominantly circular direction and are present just deep to the nipple. Their contraction is induced by cold or tactile stimuli (e.g. in suckling) causing erection of the nipple and wrinkling of the surrounding areola (***Maxwell GP, et al., 2009).***