Abstract

Breast cancer is a cancer that develops from breast tissue. Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, or a red scaly patch of skin. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin.

Risk factors for developing breast cancer include being female, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, older age, and family history.

Magnetic resonance imaging (MRI) is a relatively recent diagnostic tool for the breast, and the role of MRI in breast cancer management is evolving. As an adjunct to mammography and ultrasound, MRI can be a valuable addition to the work-up of a breast abnormality or biopsy-proven cancer. MRI has the advantages of providing a three-dimensional view of the breast, performing with high sensitivity in dense breast tissue and using non-ionizing radiation. MRI has significant disadvantages as well, including its high cost, variability in performance, and moderate specificity that, in combination with high sensitivity, often leads to unnecessary work-up.

Keywords: Role of Proton, MR-Spectroscopy, Predicting the Response, Locally Advanced Breast Cancer, Neoadjuvant Chemotherapy.

INTRODUCTION

Primary systemic therapy (PST), also known as neoadjuvant chemotherapy, is performed prior to breast cancer surgery and offers several advantages over standard postoperative chemotherapy ***(Meisamy et al., 2004).***

The use of PST permits in vivo monitoring of tumor response. Complete disappearance of tumor at surgical resection (hereafter, pathologic complete response) was associated with the best overall survival in multiple studies ***(Meisamy et al., 2004).***

Since there are many active agents available for the treatment of breast cancer, it is important to know early in the course of treatment whether the drug chosen will be effective or not. There are currently no standardized criteria that can individually enable detection of early response to PST ***(Meisamy et al., 2004).***

Conventional modalities such as physical examination, ultrasonography (US), and mammography vary in reliability for measuring tumor response ***(Segel et al., 1988; Vinnicombe et al., 1996; Junkermann and Von, 1997; Herrada et al., 1997).***

Magnetic resonance (MR) imaging is increasingly being used to evaluate locally advanced breast cancer defined as invasive carcinoma 2 cm or larger in longest diameter (LD) with or without inflammatory features ***(Meisamy et al., 2004).***

With respect to treatment monitoring, study results have shown correlation between specific MR findings and clinical response. However, changes in lesion size or dynamic contrast enhancement measured with MR imaging are not detected until at least 6 weeks following PST ***(Rieber et al., 2002).***

The ability to immediately detect response to a specific chemotherapeutic regimen would be ideal, since it would allow for optimal individualization of chemotherapeutic regimens for patients, with the goal of obtaining a pathologic complete response. Recently there has been an interest in the use of hydrogen 1 (1H) MR spectroscopy for the detection and monitoring of breast cancer ***(Meisamy et al., 2004).***

Proton (hydrogen 1 [1H]) magnetic resonance (MR) spectroscopy provides biochemical information about the tissue under investigation ***(Bartella and Huang, 2007).***

Several studies over the past decade documented that tCho is specific to malignancy and can be used to differentiate cancerous from benign tissues ***(Sharma et al., 2008)***

The water suppressed in–vivo H1 MR spectrum acquired from malignant breast lesion is characterized by an intense peak at 3.22 ppm corresponding to several Cho containing compounds ***(Sharma et al., 2008).***

So an early decrease in the concentration of tCho could allow us to identify an early response to PST ***(Meisamy et al., 2004).***

AIM OF THE WORK

To clarify the role of proton MR-spectroscopy in predicting the response of locally advanced breast cancer to neoadjuvant chemotherapy.

ANATOMY OF THE BREAST

Development of the breast

The mammary line (crest, ridge) is an ectodermal (epidermal) thickening that appears during the 4th–5th week of development. It extends from axilla to groin, on each side of the body **(Fig.1)**. Only a small portion of the line persists in the thoracic region ***(Sadler, 2004).***

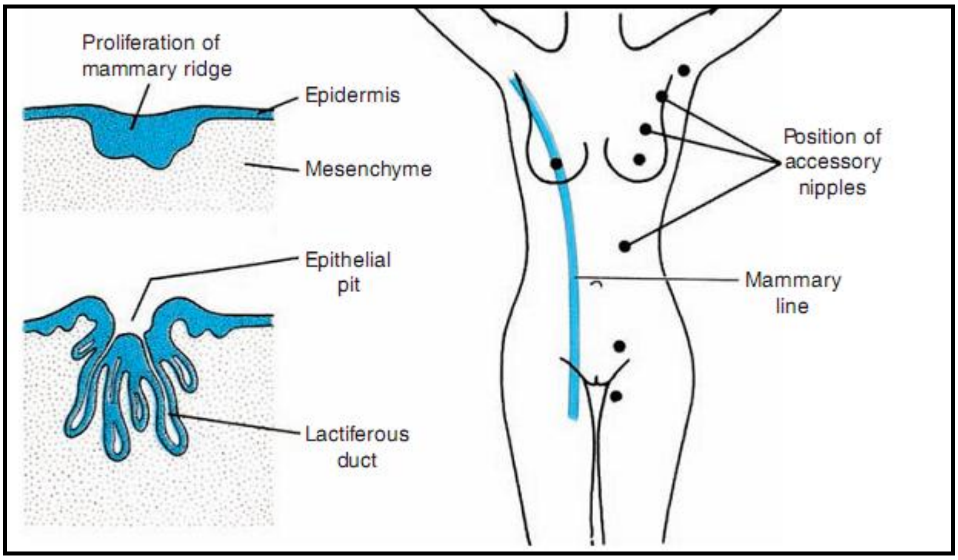

Figure (1): The position of the mammary line ***(Sadler, 2004).***

Invasion of the underlying mesenchyme (dermis) in the 6th week gives rise to the mammary buds. These lengthen, branch and are canalised to form the lactiferous ducts. The lactiferous ducts come together in a depression on the surface of the skin called the mammary pit. Shortly after birth the pit is converted to the nipple ***(Moore and Persaud, 2003).***

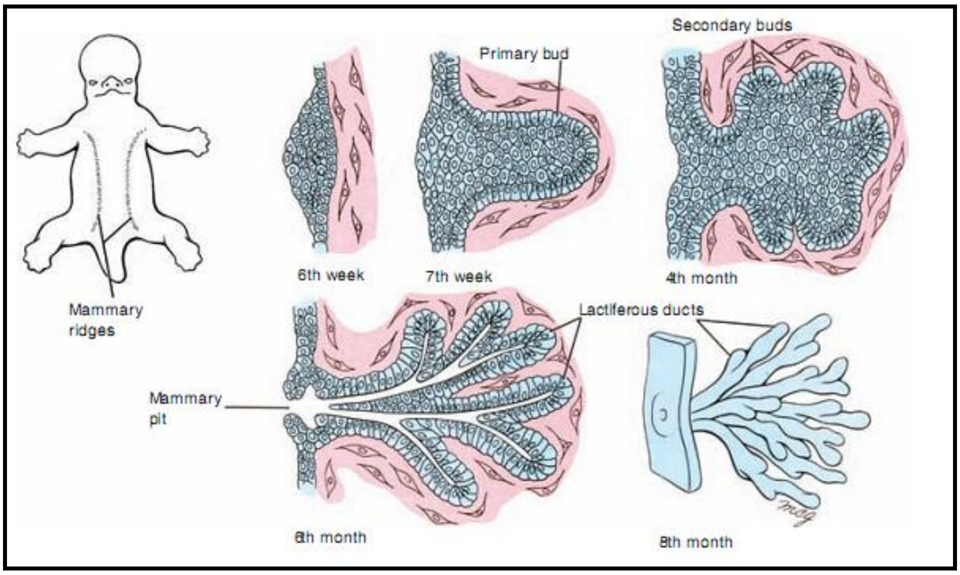

Figure (2): The development of the mammary gland tissue ***(Larsen, 1993).***

Persistence of remnants of the mammary line may give rise to accessory nipples (polythelia). They are found along of the mammary line and are commonly mistaken for moles. An extra breast develops if a remnant of the mammary line completely develops into a breast (polymastia). Amastia is the congenital absence of the breast. It can be either unilateral or bilateral and is very rare. In amazia there is absence of breast tissue but the nipple is formed ***(Larsen, 1993).***

Basic anatomical considerations

The female breast lies on the anterior thoracic wall with the base extending from the second to sixth rib. The anatomic boundaries of the breast are from the level of the second or third rib superiorly to the inframammary fold inferiorly, and its transverse boundary from the lateral border of the sternum medially to the mid-axillary line laterally. The breast tissue frequently extends into the axilla as the axillary tail of Spence **(Fig. 3)** ***(Sonali and Richard, 2011).***

The axillary tail is a prolongation of the superolateral quadrant to wards the axilla along the infero lateral edge of pectoralis major, from which it projects a little, and may extend through the deep fascia up to the apex of the axilla ***(Michael, 2000).***

The nipple projects from the centre of the breast anteriorly. Its level in the thorax varies widely, but is at the fourth inter costal space in most young women. The areola is a disc of skin, which circles the base of the nipple, varying in color from pink to dark brown depending on parity and race ***(Michael, 2000).***

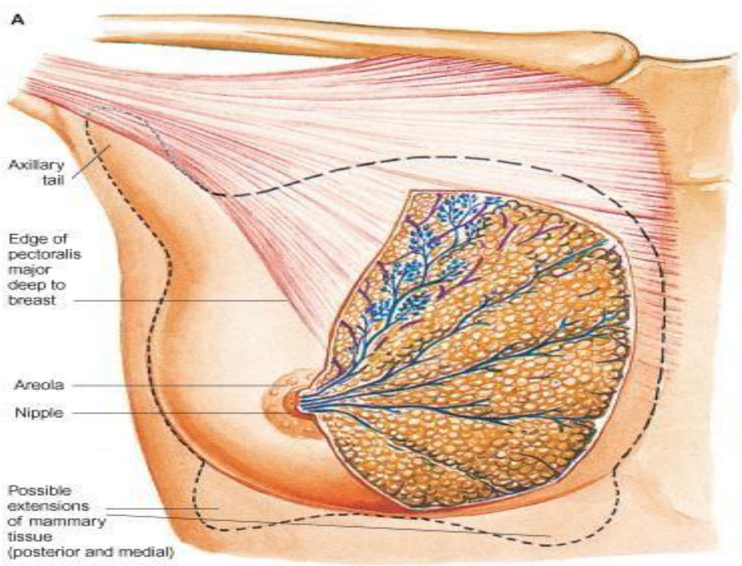

Figure (3): The macroscopic structure of the breast ***(Michael, 2000).***

The structural component of the breast

The breast is composed of two main elements; parenchyma (function a lelement) and stroma (supportive element). The function alfibro glandular tissue is composed of 15-20 lobes which arranged in radiating fashion ***(Glenn, 2001).***

Each lobe is drained by a single major lactiferous duct that opens onto the nipple. Each lobe is made up of several lobules, which drain via a branching arrangement of ducts (lobular ducts) to the single lobar duct. Each lobular duct drains several acini which are blind saccules, from which the milk is secreted during lactation ***(Michell et al., 2003).***

The basic functional unit of the breast is called the terminal ductal- lobularunit (TDLU), which is composed of a small segment duct and a cluster of alveoli (acini) **(Fig.2)** ***(Rosen, 2001).***

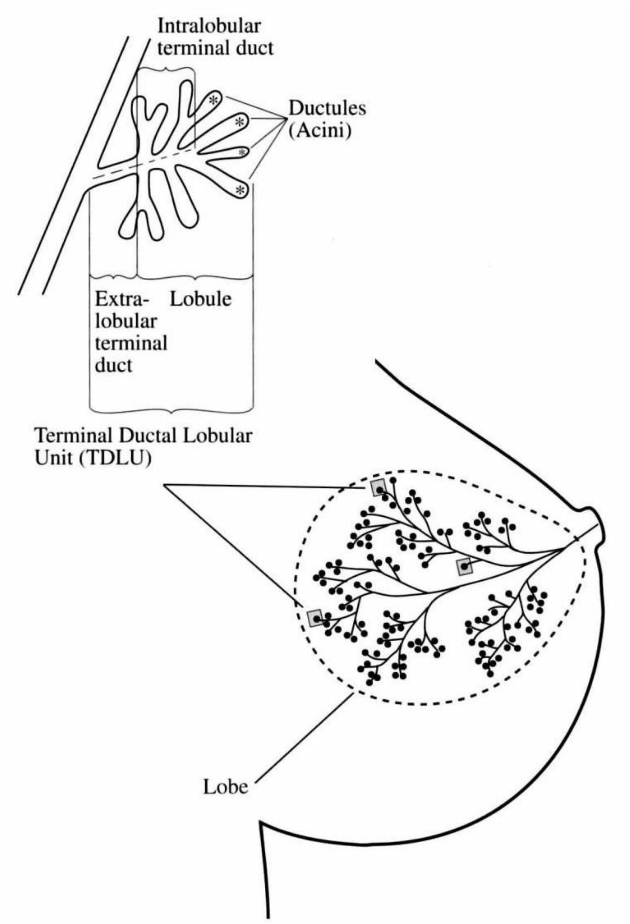

Figure (4): Anatomy of the human breast, a lobe and a TDLU ***(Reinikainen, 2003).***

The TDLU is the most important structure in the breast. It is the glandular unit, and it is postulated that most cancers a rise in the terminal duct either inside or just proximal to the lobule. In addition to cancer, most of benign lesions that develop in the breast develop in the TDLU **(Fig.4)** ***(Kopans, 2004).***

The supportive tissue (stroma) consists of connective tissue containing blood vessels, nerves, lymphatics and variable amount of adipose tissue. Adipose tissue is bounded beneath the skin and glandular tissue and fills the spaces between the lobules **(Fig. 5)** ***(Glenn, 2001).***

There is aunique variations of the connective tissue septae within the breast that forms a fibrous skeleton, these connective tissue septaeare collectively called Cooper`s ligaments ***(Glenn, 2001).***

These ligaments are attached anteriorly to the skin of the breast and posteriorly to the pectoral fascia providing a supportive frame work between the two fascial layers ***(Michael, 2000).***

The relative abundance of the parenchyma and stroma varies according to age, parity and other factors ***(Michell et al., 2003).***

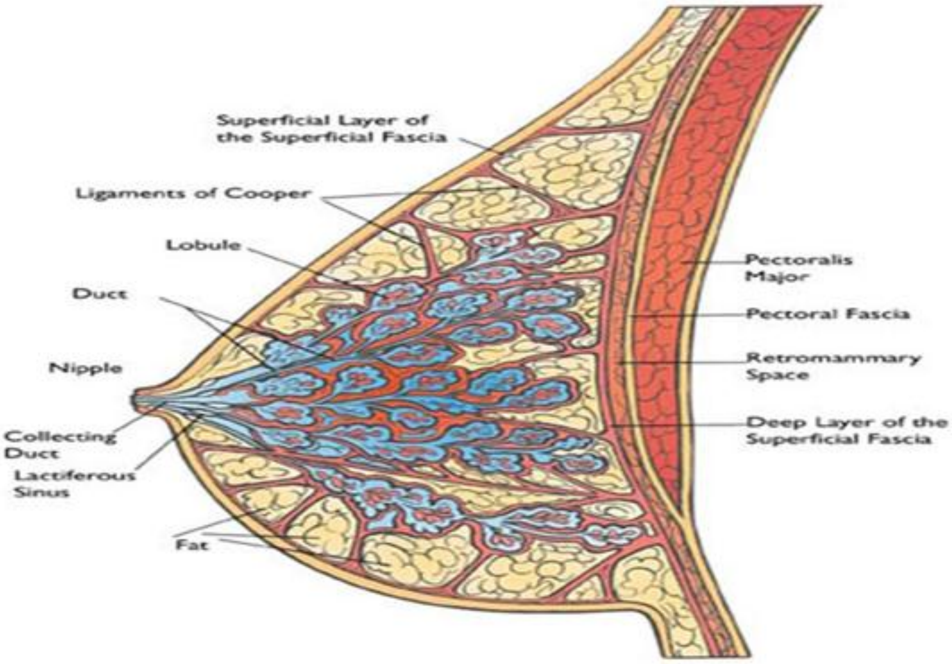

Figure (5): Normal anatomic components ofthe female breast ***(Michael, 2000).***

Physiologic changes of the breast

The breast is affected byphysiologic changes in breast morphology and function throughout life from menarche to menopause, and during each menstrual cycle. These changes are based on hormonal activity, mainly by prolactin, estrogen and progesterone. At menarche, the main events included development and growth of ductal and lobular units. At pregnancy, are markable rise of hormone levels induces growth and secretory activity of the breast. Postmenopausally, the breast undergoes involution characterized by atrophy of the parenchymal structures ***(Reinikainen, 2003).***

Vascular supply of the breast

Arterial supply of the breast

It is divided into the blood supply to the skin and the mammary gland proper.

The skin of the breast is supplied by:

- Medially, branches of the anterior intercostals arteries as the vessels pass laterally supplying the intercostals muscles.
- Laterally, branches from the lateral thoracic artery, a branch of the axillary artery, and by lateral cutaneous branches of posterior intercostal arteries, the soft tissue of the mammary gland proper is supplied by

Branches of:

- The axillary artery: it gives many branches namely, the superior thoracic, the pectoral branches of the thoraco-acromial artery, the lateral thoracic (via branches which curve around the lateral border of the pectoralis major muscle supplying the lateral aspect of the breast) and the subscapular artery.
- The internal thoracic artery supplies perforating branches to the anteromedial part of the breast.
- The second to fourth anterior intercostals arteries supply perforating branches more laterally **(Fig. 6)** ***(Michael, 2000).***

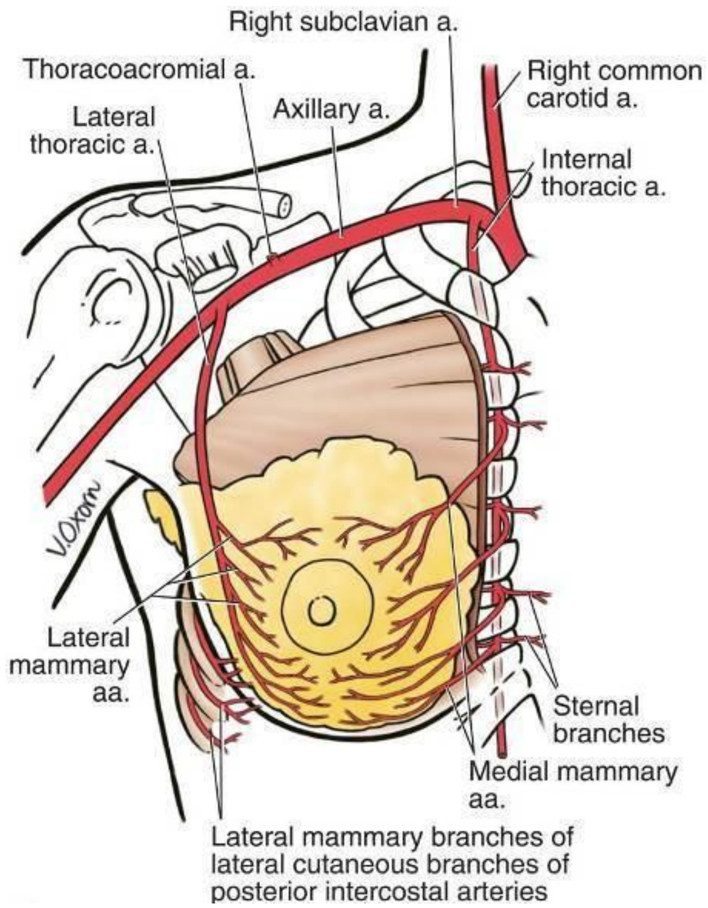

Figure (6): Arterial supply of the breast ***(Michael, 2000).***

Venous supply of the breast

The venous drain age system of the breast includes:

The intercostals veins which traverse the posterior aspect of the breast from the second or third through the sixth or seventh intercostals spaces to terminate posteriorly into the Azygos system on the right and the Hemiazygos system on the left side, terminating in the superior vena cava.

The deep venous drainage of the breast in large part parallels the pectoral branches of the thoraco-acromial artery and the lateral thoracic artery.

Superior, central and lateral aspects of the breast are drained by tributaries that enter the axillary vein. Medial aspect of the breast is drained by perforating veins of the internal mammary venous system ***(Michael, 2000).***

Lymphatic drainage

The lymphatic drainage of the breast can be very variable. There are communicating lymphatic plexi in the inter lobular connective tissue and the walls of the lactiferous ducts and the subareolar region. There is also a plexus of minute vessels on the subjacent deep fascia, but it plays little part in normal lymphatic drainage or in early spread of carcinoma. It offers an alternative route when the usual pathways are obstructed ***(Susan et al., 2005).***

The superficial lymphatics are present under the skin of the breast and a particular concentration in the subareolar plexus, beneath the nipple. Lymph flows unidirectionally from superficial to deep in the breast to the perilobular and deep subcutaneous plexus. Lymphinthe deep plexus then drains centrifugally from the nipple to the axillary and internal mammary chains **(Fig. 7)** ***(Rayan et al., 2004).***

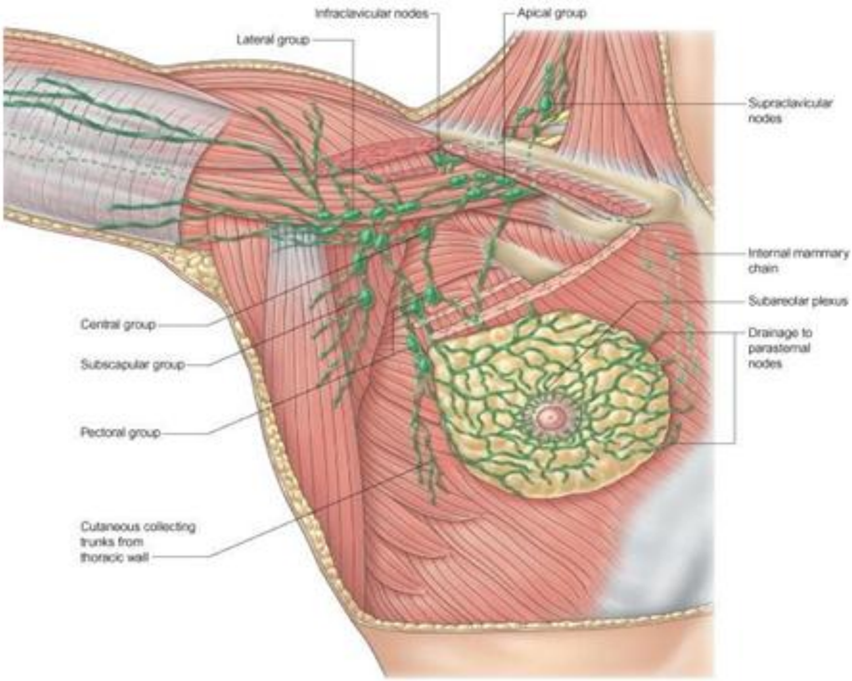

Figure (7): Lymphatic drainage of the breast.

Axillary nodes receive more than 75% of the lymph from the breast. There are 20-40 nodes, grouped artificially aspectoral (anterior), sub scapular (posterior), central and apical. Surgically, the nodes are described in relation to pectoralis minor. Those lying below pectoralis minor are the low nodes (level 1), those behind the muscle are the middle group (level 2), while the nodes between the upper border of pectoralis minor and the lower border of the clavicle are the upper or apical nodes (level 3). There may beoneor two other nodes between pectoralis minor and major. Efferent vessels directly from the breast pass round the anterioraxillary border through the axillary fascia to the pectoral lymph nodes; some may pass directly to the subscapular nodes. A few vessels pass