Abstract

Background: BIRADS III and IV lesions are a clinical dilemma as they need either follow up or biopsy. Since 80% of lesions determined in the breast are benign upon biopsy, we need new methods for evaluation of these lesions to avoid unnecessary breast interventions. MR spectroscopy is a promising new technique which can be used to improve the diagnosis of breast lesions classified according to BIRADS category. The diagnostic value of H-MRS is typically based on the elevation of choline compounds which are the markers of malignancy and aid in the differentiation between benign and malignant breast lesions.

Aim of the Work: To assess the diagnostic value of MR spectroscopy using choline peak as a malignancy marker in diagnosis of suspicious breast lesions categorized by mammography or sonomamography as (BIRADS III, IV) and correlation with available histopathological findings, clinical data or follow up.

Patients and Methods: In this study 35 female patients classified as BIRADS III & IV by sono-mammography (Sono-MX) or sonography were examined by conventional dynamic MRI and proton MR spectroscopy using a magnet (1.5 Tesla). Single voxel technique after adequate shimming was used.

Results: A choline peak was present in 13 lesions (37.1%) of 35 and in 3 of 18 benign lesions. Calculated MR spectroscopy sensitivity was 100% and specificity 88%. Positive predictive value was 76.9%, false positive rate was 12.0%, correct classification was 91.4%**.**

Conclusion: Breast single MRS can increase the specificity of the conventional dynamic MRI in evaluating breast lesions classified as (BIRADS III and BIRADS IV) and hence reduced the number of unnecessary biopsies.

KEY WORDS: **MR SPECTROSCOPY, CHOLINE, SUSPICIOUS,BIRADS III & V.**

Introduction

Breast cancer is the most common cancer among women in Arab countries with a young age of around 50 years or even younger at presentation. Locally advanced disease is very common and total mastectomy is the most commonly performed surgery ***(Saghir et al., 2007).***

Traditional approaches to assess breast lesions are routine screening methods, such as ultrasonography (US) and mammography. Mammography provides a widely available, reliable and cost-effective screening tool, however has decreased efficacy in patients with dense breasts, patients with silicone implant and patients that have previous surgery. US classification of benign and malignant breast lesions is of low specificity about 30% and ultimately requires histology for confirmation ***(Aydin et al., 2013).***

MRI is playing an increasingly important role in the screening of women at high risk for breast cancer. One drawback of the technology, however, has been a considerable number of breast biopsy procedures recommended on the basis of imaging findings, which turn out to be benign. With MR spectroscopy, the radiologist is able to see the chemical make-up of a tumor, so in most cases, he or she can tell without biopsy whether or not the lesion is cancerous ***(Bartella et al., 2006).***

H-MRS allows non-invasive molecular analysis of biologic tissues and has been suggested as an adjunct to MR examination to improve the specificity of distinguishing benign from malignant breast masses classified according to BIRADS category. The diagnostic value of H-MRS is typically based on the elevation of choline compounds which are the markers of active tumour and aid in the discrimination between benign and malignant breast lesions mainly the BI-RADS 3-5 masses ***(Aydin et al., 2013).***

Suspicious lesions may also be characterized by their cellular chemistry obtained from proton MR spectroscopy (MRS).Proton MRS analyses of the breast have shown high levels of total choline-containing compounds at 3.2 ppm in malignant lesions but low levels in normal breast tissues and benign lesions. In vivo single-voxel proton MRS may be a sensitive diagnostic tool in patients with breast cancer ***(Shin et al., 2012).***

Recent evidence suggests that MR Spectroscopy, if incorporated into a standard MRI examination, may be effective in increasing the specificity and positive predictive value of lesion evaluation. For benign lesions where MRI is inconclusive, MRS may eliminate the need for biopsy by demonstrating the lack of a choline resonance ***(Cecil et al., 2001).***

With the addition of MR spectroscopy to breast MRI exam, the number of biopsies recommended on the basis of MRI findings decreased significantly. These results should encourage more women to take this potentially life-saving test ***(Bartella et al., 2006).***

AIM OF THE WORK

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Chapter 1

ANATOMY OF THE BREAST

The breast consists mainly of fat and glandular tissue, the latter varying throughout life, in response to female hormones ***(Butler et al., 2011).***

The adult female breast lies between the second and sixth/seventh ribs. The base of the breast extends from the sternal border medially to the mid axillary line laterally and is encompassed by the superficial and deep fascia of the chest wall. Two-thirds of the breast lies anterior to the pectoralis major; the remainder lies anterior to the serratus anterior. A prolongation of the upper outer quadrant of the breast, referred to as the tail of Spence, extends into the axilla ***(Soran et al., 2016).***

Components of the Breast

Skin: – The skin is the most superficial layer of the breast. The dermis merges with the superficial fascia.

Superficial fascia: – This layer lies just beneath the skin. It is continuous with the superficial abdominal and cervical fascia. Along with the deep fascia, it envelopes the breast parenchyma

Breast parenchyma: – The parenchyma is composed of three principal tissue types: glandular epithelium, fibrous stroma, and supporting structures and fat (Fig. 1) ***(Soran et al., 2016)***.

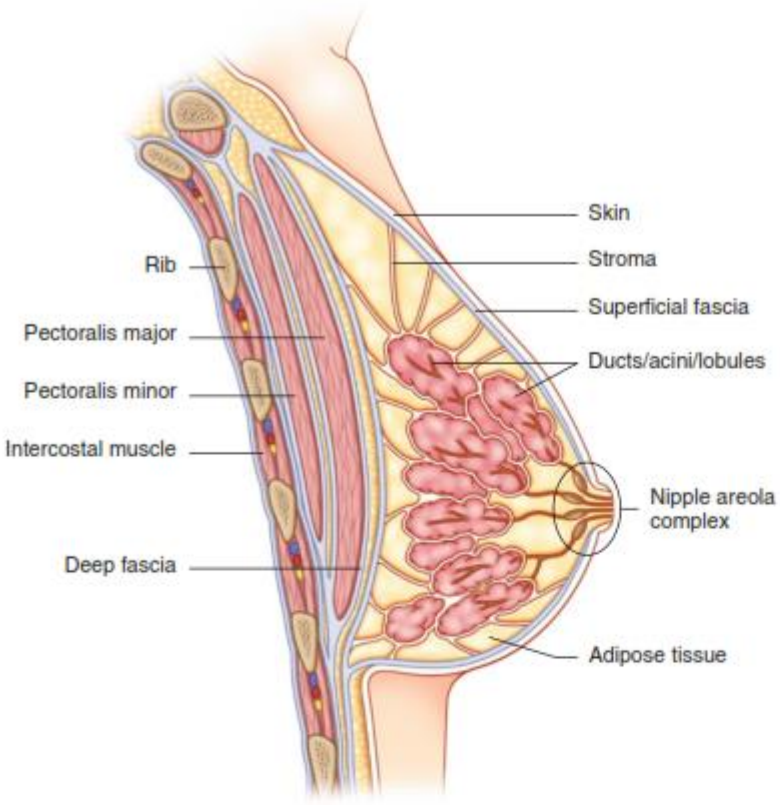

Fig. (1): Component of the breast ***(Soran et al., 2016).***

The skin of the breast is thin and contains hair follicles, sebaceous glands and apocrine sweat glands. The nipple is a round fibro-muscular papilla projecting from the center of the breast nearly at the level of fourth intercostal space in the non-pendulous breast. The areola is a small circular area of pigmented skin surrounding the nipple and contains enormous sebaceous glands [Montgomery's glands] ***(Morris et al., 2005)*** with secondary papillae, and it is perforated by from fifteen to twenty orifices ***(Johnson et al., 2004).***

The fibrous stroma and supporting structures are most commonly referred to as the suspensory ligaments of Cooper. These ligaments are fibrous bands of connective tissue that travel through the breast and insert into the dermis. Tumor involvement and contraction of these bands are responsible for the puckering noted at the site of a palpable breast lump ***(Soran et al., 2016).***

The parenchyma is divided into 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 stromal tissue (Fig. 2) ***(Morris, 2005).***

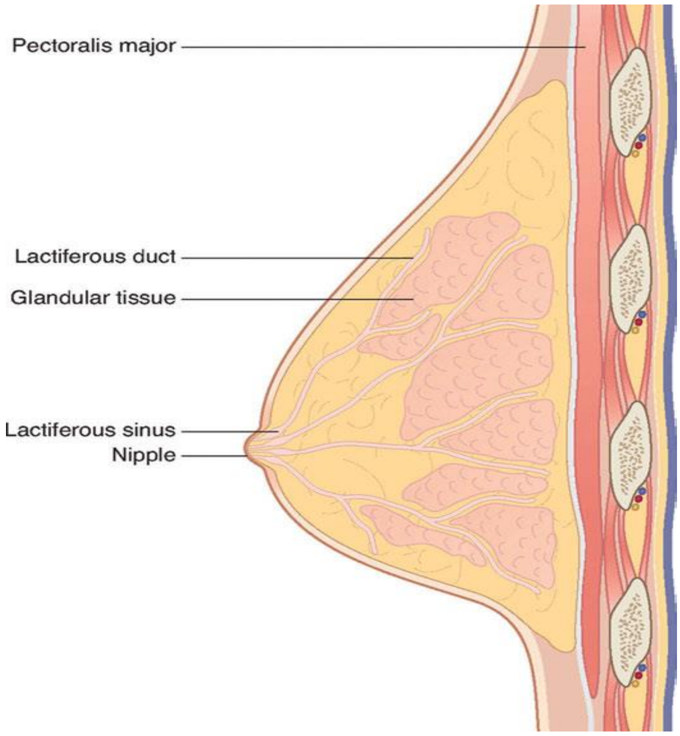

Fig. (2): Line diagram showing anatomical detail in the mediolateral oblique view, as seen on this standard mammographic projection. The breast is seen to consist mainly of fat and glandular tissue, and is entirely enveloped in chest wall fascia, which forms septae called Coopers suspensory ligaments. These support the breast, running from the fascia of the pectoralis muscles posteriorly to the skin anteriorly ***(Butler et al., 2011).***

The remainder of the breast is composed of adipose tissue (fat). The proportion of fat to glandular tissue increases with age and is maximal in the postmenopausal breast.

Nipple - areola complex:- each lobe of the breast leads to a ductal structure that then widens to form a large lactiferous duct (2–4 mm) that continues to form a sinus. The sinus is lined with stratified squamous epithelium. This sinus then narrows as it passes into the ampulla of the nipple (0.4–0.7 mm). The areola comprises a combination of sebaceous, sweat, and accessory glands that form the Montgomery tubercles. Smooth muscle fibers are contained in the areola and extend into the nipple, and these fibers are responsible for nipple erection. Erection is stimulated by the sensory nerve endings and Meissner's corpuscles, which are located within the dermis of the nipple.

Whereas all components of the breast are influenced by female hormones, the glandular tissue is most sensitive. Very dramatic and totally normal changes can occur in the consistency of the breasts during the menstrual cycle. These changes are most evident just prior to menstruation when levels of estrogen and progesterone are peaking. Few days after menstruation, hormone levels are at their lowest and the breast becomes softer and less tender. This is the recommended time to perform breast self-examination and to have a mammogram ***(Ramsay et al., 2005).***

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 pre-menstrually 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).***

Neurovascular Structures

Arterial: The arterial blood supply to the breast comes primarily from three sources:

(1) Anterior perforators of the internal mammary artery (responsible for approximately 60 % of the breast, mostly medial and central)

(2) Branches from the axillary artery, such as the highest and lateral thoracic, and the thoracoacromial artery (responsible for approximately 30 % of the breast, mostly the upper outer quadrant)

(3) Lateral branches of the intercostal arteries ***(Soran et al., 2016).***

Venous: Venous drainage typically mimics the arterial supply. Thus, the primary venous drainage consists of: (1) internal mammary perforating branches, (2) tributaries of the axillary vein, and (3) branches of the intercostal veins (Fig. 3).

Nervous: The sensory nerve supply to the breast is principally derived from the lateral cutaneous branches of the third through sixth intercostal nerves. Cranially, some sensory innervation is supplied by cutaneous branches of the cervical plexus. The nipple-areola complex is innervated by the fourth intercostal nerve ***(Soran et al., 2016).***

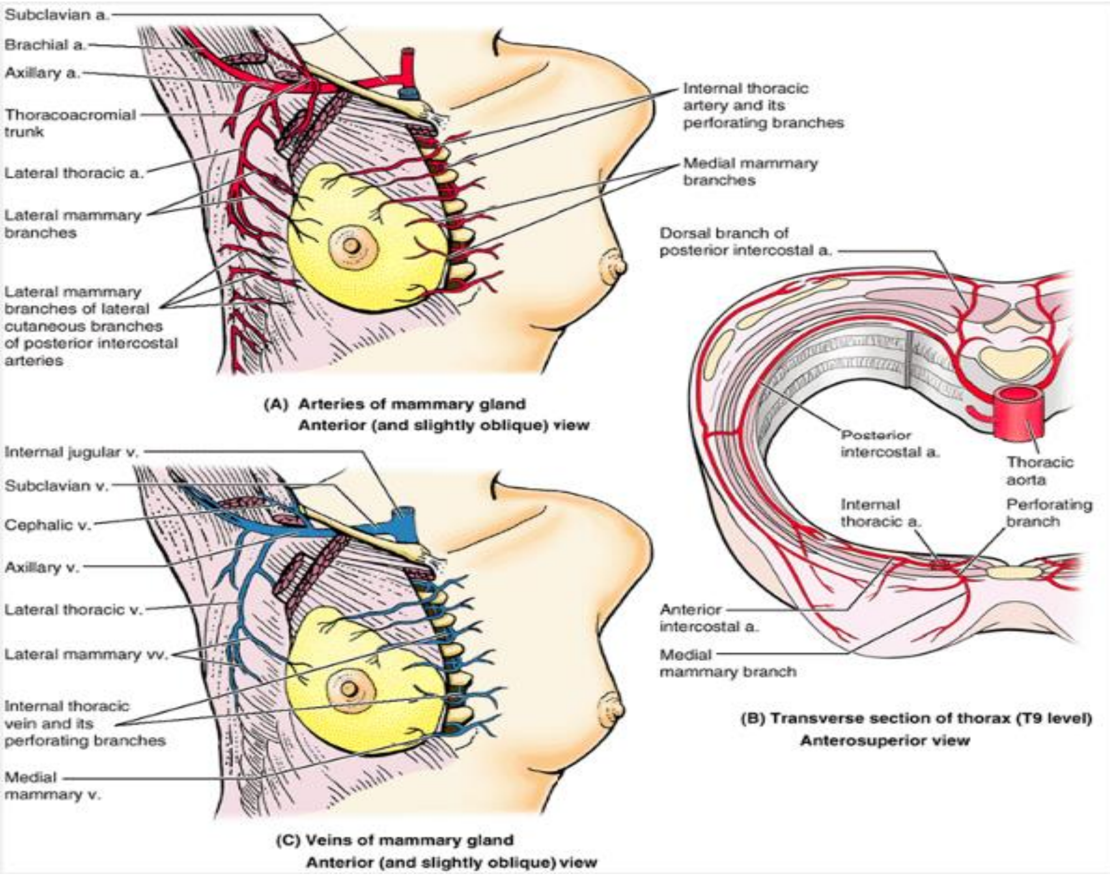

Fig. (3): Arterial supply and venous drainage of breast
(Moore et al., 2006).

Lymphatic drainage

The axillary lymph nodes vary in number from 20 to 30 and are divided into five anatomical groups (Fig. 4) ***(Ellis, 2006).***

Lateral group

- Four to six nodes.
- Posterior and medial to the axillary vein.

Anterior (pectoral) group

- Usually four to five nodes.
- Along the inferior border of pectoralis minor adjacent to the lateral thoracic vessels.

Posterior (sub scapular) group

- Six to seven nodes.
- Lie along the sub scapular vessels.

Central group

- Three or four large nodes.
- In the axillary fat pad.
- Receive efferent lymphatic from the first three groups of nodes.
- Drain into apical nodes.

Apical group

- Six to twelve nodes.
- Posterior to and above the pectoralis minor along the medial aspect of the axillary vein.
- Receive efferent from the other lymph node groups, lymphatics running along the cephalic vein, and some direct drainage from the upper periphery of the breast.

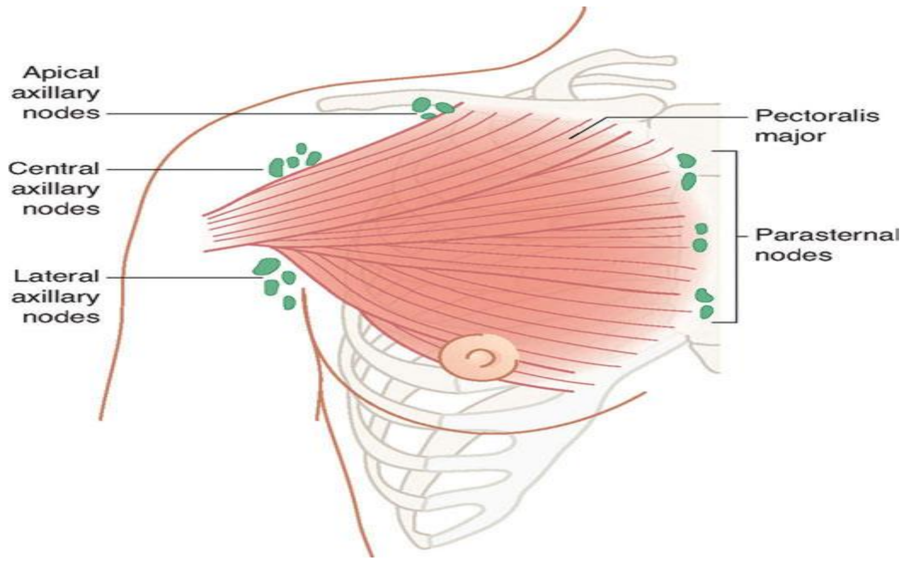

Fig. (4): Lymphatic drainage of the breast ***(Butler et al., 2011).***

Efferent from the apical nodes unite into the subclavian trunk. On the left side, this trunk usually drains directly into the thoracic duct. On the right side, the subclavian trunk may empty directly into the jugulosubclavian junction or into a common right lymphatic duct. A few efferent channels usually reach the inferior deep cervical nodes directly.

Clinicians and pathologists often define metastatic axillary node spread simply into three levels:

- Level I: nodes inferior to pectoralis minor
- Level II: nodes behind pectoralis minor
- Level III: nodes above pectoralis minor.

The internal thoracic (internal mammary) lymph nodes are small, often only 2–3mm in diameter, and lie along the internal thoracic vessels 2–3cm from the sternal edge. Usually three to five of these nodes are found on either side. These nodes drain the anterior chest wall, anterior portion of the diaphragm, upper portion of the rectus sheath and muscle, and the superior portion of the liver, as well as the inner aspect of the mammary gland ***(Ellis, 2006).***

The intercostal nodes lie near the rib heads. They receive deep lymph vessels from the posteromedial aspect of the chest and some drainage from the lateral extremity of the mammary gland (Fig. 5) ***(Ellis, 2006).***

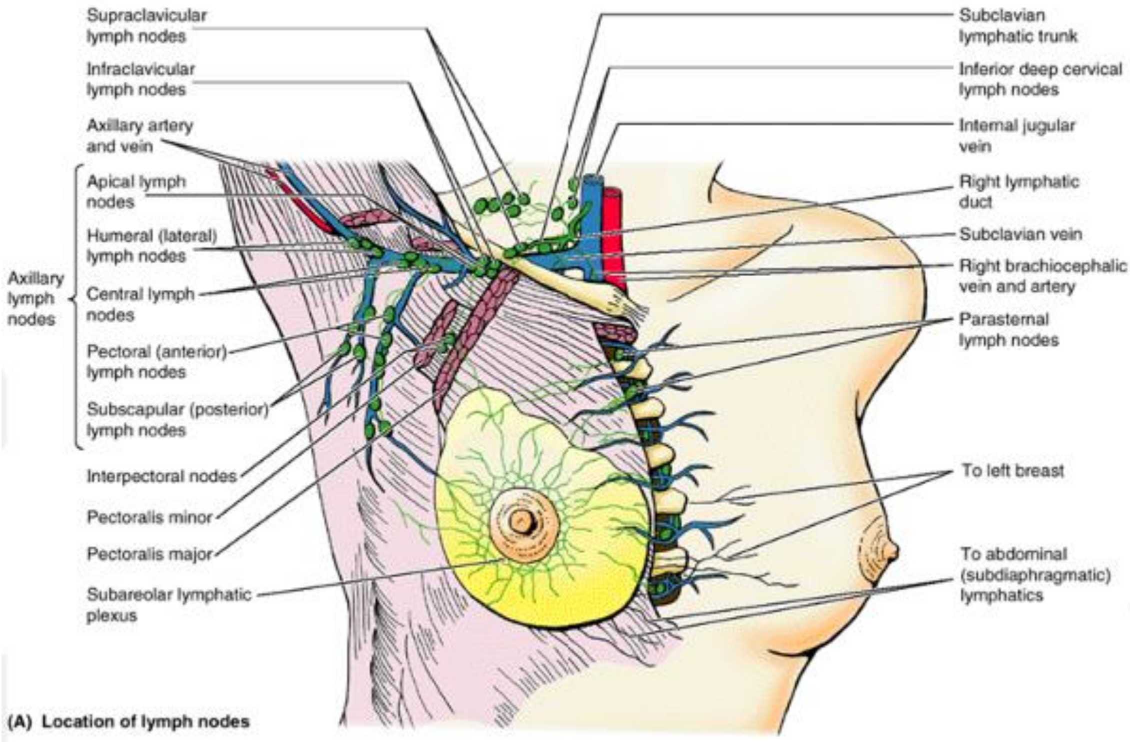

Fig. (5): Lymphatic drainage of the breast ***(Moore et al., 2006).***

About 75% of all lymphatic drainage of the breast passes to the axillary nodes. The remainder principally drains to the internal thoracic nodes. Any part of the breast may drain to either group, though there is a greater tendency for tumors situated in the medial part of the breast to disseminate to the internal thoracic nodes than for tumors in the lateral part of the breast ***(Ellis, 2006).***

Involvement of the supraclavicular nodes in breast cancer usually represents retrograde spread along blocked lymphatic channels when the apical axillary nodes are heavily involved. However, efferent channels do pass directly from these nodes to the inferior deep cervical chain so that involvement of cervical nodes may occur via this route ***(Ellis, 2006).***

Lymphatics do not normally drain to lymphatics across the opposite side of the body; early lymphatic spread of a tumor from one breast to another does not occur. Such bilateral cases represent synchronous or early metachronous double primary tumors. In very advanced cases, however, extensive blockage of lymphatic channels allows subcutaneous lymphatic permeation to occur to the opposite side ***(Ellis, 2006).***

Axilla:

The axilla is an important component of breast anatomy. Directly contiguous with the breast, the lymph nodes within the axilla provide a rich drainage basin for the breast. The borders