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 an indication that they will continue to do so over the next few decades ***(Jack Cuzick, 2010)***. In the last several years, various imaging modalities including X-Ray mammography, MRI, PET and ultrasound have been used to detect and diagnose breast cancer ***(Hung et al., 2003)***.

Conventional mammography is known to have high false positive rates in the detection of breast malignancy (60-80%), resulting in unnecessary biopsies being performed. In recent years, MR techniques have shown strong potential to improve the sensitivity and the specificity in the diagnosis of breast cancer. Dynamic contrast enhanced MR imaging has demonstrated high sensitivity in the detection of suspicious breast lesions ***(O'Heab et al., 2002).***

Proton MR Spectroscopy (MRS) allows non invasive molecular analysis of biologic tissue ***(Sardenelli et al., 2009).*** It shows excellent specificity in the detection of breast lesions. Choline is generally undetectable in normal breast tissue, increased levels of Choline compounds in a tumor, is thought to be an indicator of the activity of that tumor, suggesting that it is malignant. This eliminates the need for biopsy, reduce patient morbidity, and save unnecessary cost and time for both the

patient and the medical staff. MR Spectroscopy can also be used to gauge the effect of chemotherapeutic agents in patients with locally advanced breast cancer ***(Tuzaki, 2008)*** and for early detection of recurrent breast cancer based on metabolic profiles by using the combination of two advanced analytical methods NMR (Nuclear Magnetic Resonance) and MS (Mass Spectrometry) ***(Gowda et al., 2010)***.

In recent years, yet another method, one that uses dynamic T2-Weighted first-pass perfusion imaging, has been proposed. Unlike normal tissues, perfusion in tumors is intense and fast. The immature blood vessels of malignant tumors differ from normal vessels by being "much leakier" (i.e. having higher permeability). Differences in cell density are also important. Cancer cells are more crowded than normal ones. Contrast agents, therefore, slowly fill up the larger empty spaces in normal tissues, compared to fast fill up of the lower extracellular volume fraction for cancerous ones ***(Barker, 2013).***

That is the concept of MR Perfusion imaging, which if performed immediately after dynamic contrast enhanced T1-Weighted imaging, can be used to differentiate between benign and malignant tumors with a high degree of certainty ***(Barker, 2013).***

However, MR Spectroscopy and MR Perfusion, have false negative results in the diagnosis of malignant breast

disease. To overcome their fallacies, combining both techniques has been studied. The results of these studies showed to have 100% specificity in the detection of breast malignancy, with the total imaging time being less than 40 minutes, and the total dosage of contrast medium, being no more than 0.2 mmol per kilogram body weight ***(Hendrick, 2010).***

AIM OF THE WORK

To detect the value of combined Perfusion MR and MR Spectroscopy in the characterization of suspicious breast masses.

Key Words:

Breast tumors, MR imaging, MR Spectroscopy and MR Perfusion.

ANATOMY OF THE BREAST

The breast overlies the second to sixth ribs on the anterior chest wall. It is hemispherical with an axillary tail and consists of fat and a variable amount of glandular tissue. It is entirely invested by the fascia of the chest wall, which splits into anterior and posterior layers to envelop it. The fascia forms septa called coopers ligaments, which attach the breast to the skin anteriorly and the fascia of pectoralis posteriorly. They also run through the breast, providing a supportive framework between the two fascia layers. The pigmented nipple projects from the anterior surface of the breast. It is surrounded by the pigmented areola and its position is variable, but it usually lies over the fourth intercostal space in the non-pendulous breast ***(Ryan and McNicholas, 2004) (Figure 1).***

The internal architecture of the breast is arranged into 15-20 lobes, each of which is drained by a single major lactiferous duct that opens on to the nipple. Each lobe is made up of several lobules, each of which drains several acini. The lobules drain via a branching arrangement of ducts to the single lobar duct. Each lobule drains several acini-these are blind saccules into which milk is secreted during lactation. The glandular tissue of the acini and the ductal tissue draining them comprise the breast parenchyma. The fat surrounding the Parenchymal structure and the fibrotic framework of the breast constitute the stroma. The relative abundance of parenchyma

and stroma varies according to age and other factors ***(Ryan and McNicholas, 2004).***

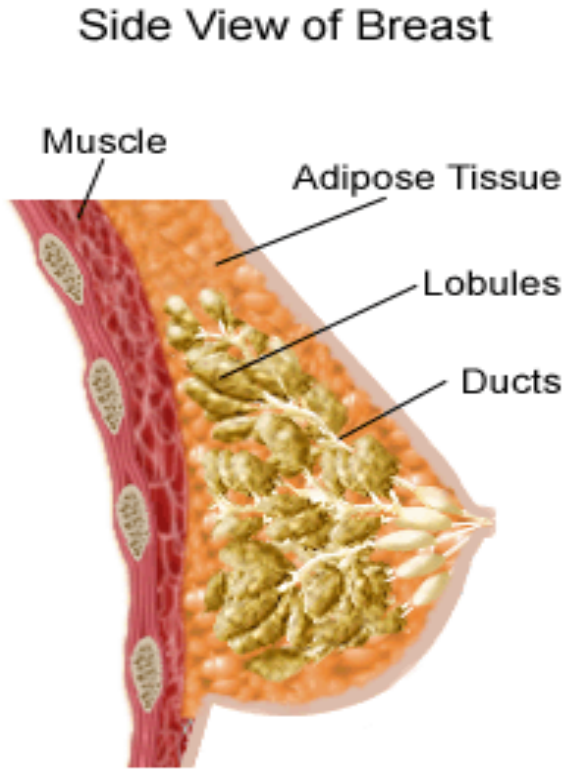


Figure (1): Normal breast anatomy ***(Nagin, 2008).***

Blood Supply

The blood supply of the breast is a rich anastomotic network derived from the axillary, internal thoracic (or internal mammary in the old nomenclature) and intercostal arteries ***(Harold, 2006).***

The largest vessels arise from the internal thoracic artery, the perforating branches of which pierce the chest wall adjacent to the sternal edge in the first to fourth intercostal spaces. The

vessel in the second space is usually the largest of these ***(Harold, 2006) (Figure 2).***

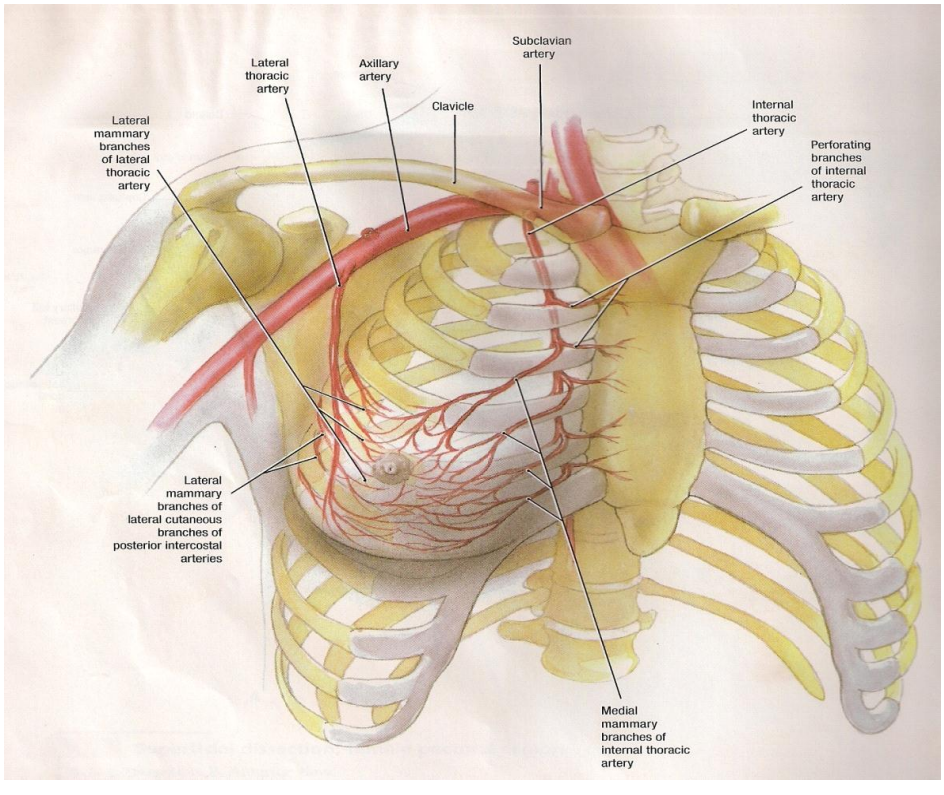


Figure (2): Blood supply to the Breast ***(Harold, 2006).***

Lymphatic drainage

The breast lymphatics drain by way of three major routes: axillary, internal mammary and transpectoral (intercostal lymph nodes) ***(Rubin and Hansen, 2013).***

A- The axillary lymph nodes

They vary in number from 20 to 30 and are divided into five anatomical groups ***(Rubin and Hansen, 2013).***

a) Lateral group

- Posterior and medial to the axillary vein ***(Rubin and Hansen, 2013).***

b) Anterior (pectoral) group

- Along the inferior border of pectoralis minor adjacent to the lateral thoracic vessels ***(Rubin and Hansen, 2013).***

c) Posterior (sub scapular) group

- Lie along the sub scapular vessels ***(Rubin and Hansen, 2013).***

d) Central group

- In the axillary fat pad.
- Receive efferent lymphatic from the first three groups of nodes.
- Drain into apical nodes ***(Rubin and Hansen, 2013).***

e) Apical group

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 ***(Rubin and Hansen, 2013).***

Efferent from the apical nodes unites 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 ***(Rubin and Hansen, 2013).***

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

- Level I (low-axilla): lymph nodes lateral to the lateral border of the pectoralis minor muscle.
- Level II (mid-axilla): lymph nodes between the medial margin of the pectoralis minor muscle and the interpectoral (Rotter's) lymph nodes.
- Level III (apical axilla): lymph nodes medial to the medial margin of the pectoralis minor and inferior to the clavicle. These are also known as apical or infraclavicular nodes. Metastases to these nodes portend a worse prognosis. ***(Rubin and Hansen, 2013) (Figure 3).***

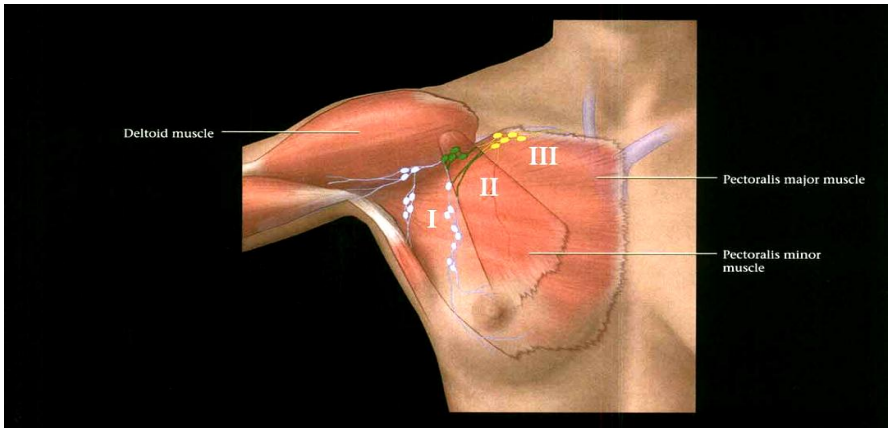


Figure (3): Level I nodes (white) are lateral /inferior to pectoralis minor. Level II nodes (green) are deep /posterior to pectoralis minor. Level III nodes (yellow) are medial and superior to pectoralis minor ***(Berg et al., 2006).***

B- The internal thoracic (internal mammary) lymph nodes

These 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 ***(Rubin and Hansen, 2013).***

C- The intercostal nodes

They 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 ***(Rubin and Hansen, 2013).***

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 ***(Rubin and Hansen, 2013).***

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 ***(Rubin and Hansen, 2013).***

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 ***(Rubin and Hansen, 2013).***

The sentinel lymph node

The sentinel node was defined by Morton et al., as any lymph node receiving direct lymphatic drainage from the primary tumor, and there for is the first node to become involved when a tumor metastasizes ***(Santosh and Mohamed, 2008).***

The concept behind sentinel lymph node biopsy is that lymphatic metastases occur in an orderly manner and that the sentinel lymph node status predicts the histological status of the regional lymph node. If the sentinel node does not contain metastases, the draining nodal basin is highly unlikely to harbor metastases and complete nodal dissection is not required ***(Santosh and Mohamed, 2008).***

There are varying methods of sentinel lymph node identification either preoperative methods or intra operative methods. The preoperative methods include injection methods by injection of blue dye or radio colloid and preoperative imaging of sentinel node, on the other hand the intraoperative methods include intraoperative periareolar injection of blue dye to be followed with gamma camera. The other is lymph node biopsy and direct intraoperative histopathological lymph node examination ***(Santosh and Mohamed, 2008).***

Age Changes in the Breast

During puberty, each menstrual cycle stimulates proliferation and active growth of breast tissue. The breast development is concerned with growth of the ductile system and the formation of ductile buds. The surrounding fat pads also develop, giving the breast size and shape ***(Brown, 2005) (Figure 4).***

Apart from the situation during pregnancy and lactation, Parenchymal atrophy starts in early adulthood and is accelerated at the menopause, with diminishing amounts of glandular tissue and an increasing amount of fat ***(Brown, 2005).***

Hormonal changes of the Breast:

Breast tissue is very sensitive to hormonal changes, especially the hormonal changes of early pregnancy. For many women this is the first sign of pregnancy. The breasts are capable of full lactation from 16 weeks of pregnancy onwards,

but women experience differing rates of growth and breast development during pregnancy ***(Brown, 2005) (Figure 5).***

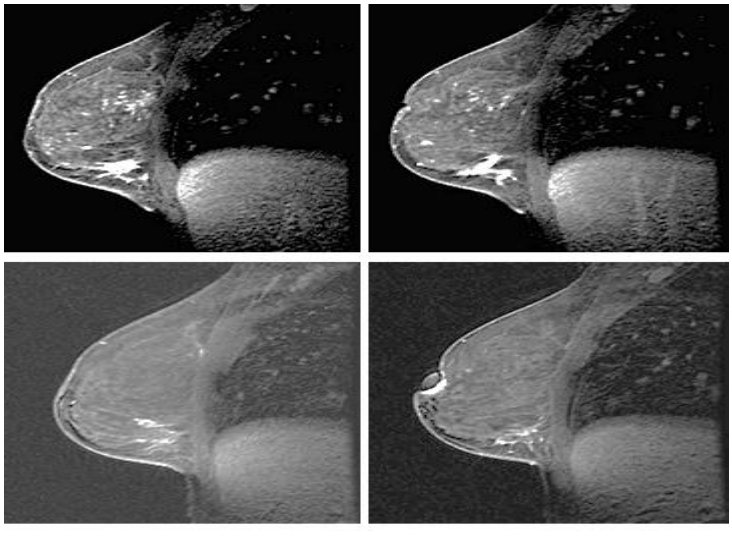


Figure (4): (A and B) Initial study in the fourth week of the menstrual cycle in a premenopausal woman. (C and D) Follow-up examination in 2 months in the second week of the cycle shows marked decrease in the overall enhancement ***(Morris, 2005).***

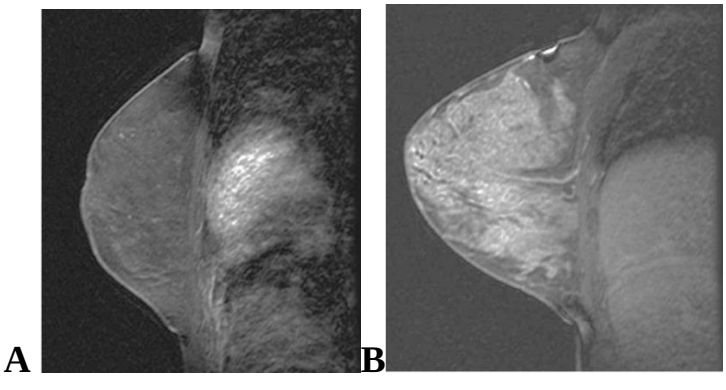


Figure (5): (A) Prior MRI examination in a 33-year-old woman who was on screening protocol. No significant enhancement is identified. (B) The same patient is reimaged while lactating. Note parenchymal proliferation as well as intense enhancement of the lactating breast tissue ***(Morris, 2005).***

Normal MRI of the breast:

Normal glandular parenchyma has intermediate signal intensity on TI- and T2-weighted sequences, whereas fat is of high signal the fibrous trabeculae are readily appreciated as fine low-signal-intensity structures traversing the subcutaneous fat ***(Figure 6).*** Low axillary and intramammary lymph nodes can be recognized through their characteristic bean shape and central fatty hilum ***(Figure 7).*** The skin is of intermediate signal and uniformly thin except in the areolar region where it may approach a few millimetres in thickness ***(Sutton, 2007).***

After intravenous gadolinium, the nipple, blood vessels and lymph nodes normally enhance. The glandular parenchyma can also enhance gradually especially in the second half of the menstrual cycle, reflecting normal hormonal–induced glandular proliferation. This enhancement is often diffuse and rather patchy ***(Sutton, 2007).***

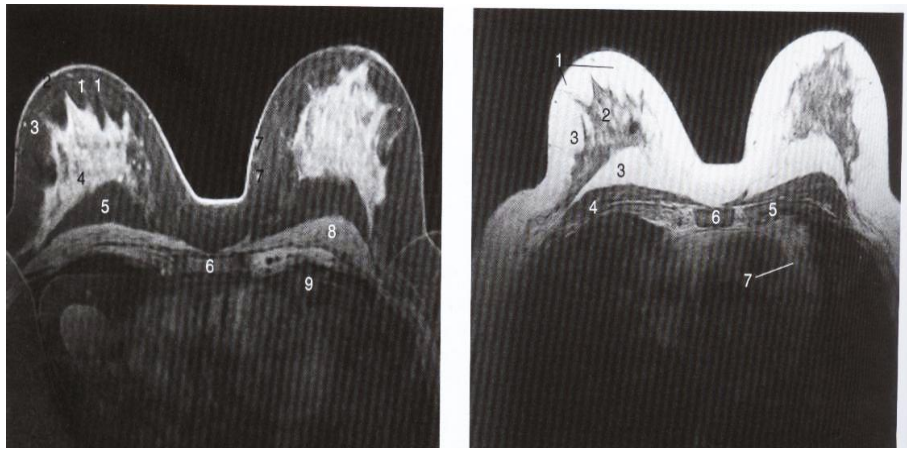


Figure (6): (A) T1-weighted, fat-saturated, gadolinium-enhanced Note- fat is dark and muscles are bright, enhancing breast tissue. B) T2-weighted image. Note- fat is bright, fibro-glandular tissue is dark.

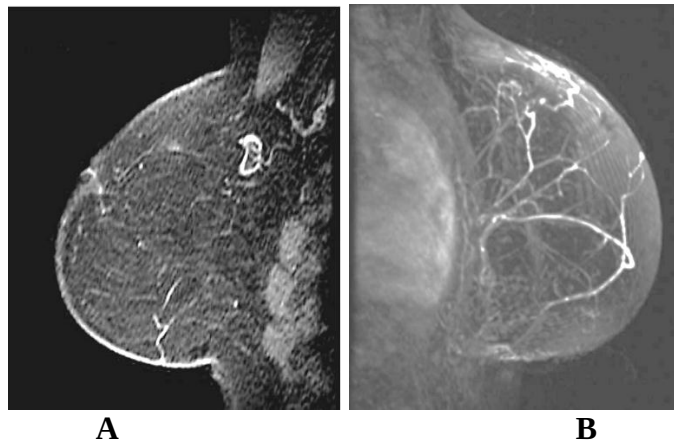
Image (A)

1. Cooper's ligament.
2. Skin.
3. Subcutaneous fat.
4. Enhancing Fibroglandular breast tissue.
5. Retroglandular fat.
6. Sternum.
7. Enhancing vessels.
8. Pectoralis major muscle.
9. Lung.

Image (B)

1. Copper's ligament.
2. Fibroglandular tissue.
3. Fat.
4. Pectoralis major muscle.
5. Costal cartilage.
6. Sternum.
7. Heart.

(Ryan and McNicholas, 2004)



A **B**

Figure (7): A. Benign lymph node with vessel radiating to hilum B. Maximum intensity projection demonstrating course of vessels ***(Morris, 2005).***