INTRODUCTION

Breast cancer is the most common invasive cancer in females worldwide. It accounts for 22.9% of invasive cancers in women. 18.2% of all cancer deaths worldwide, including both males and females, are from breast cancer ***(Yarnold et al., 2016).***

Treatment options are divided into; radiation therapy (radiotherapy) surgical treatment (Ie, lumpectomy, mastectomy and axillary lymph node dissection), Biological therapy (targeted drug therapy), hormonal therapy and chemotherapy ***(Yarnold et al., 2016).***

Research has shown that women who receive chemotherapy prior to surgery, known as Neoadjuvant chemotherapy (NAC), are more likely to achieve breast conservation than those receiving chemotherapy after surgery ***(Nola et al., 2012).***

Neoadjuvant chemotherapy (NAC) followed by surgery has been shown to be effective for locally advanced breast cancer. This treatment combination is advantageous because it can provide evidence of in vivo responsiveness to the chosen chemotherapeutic agent ***(Von Minckwitz et al., 2012).***

Magnetic Resonance Imaging (MRI) is playing a growing role in breast cancer detection, particularly for screening patients at high risk for cancer and evaluating the extent of disease in patients with a recent diagnosis of cancer ***(Saslow et al., 2014).***

Dynamic contrast-enhanced MRI (DCE-MRI) is a sensitive tool for the detection of breast cancer; the reported sensitivity is as high as 94–100%. DCE-MRI is being used as an adjunct to mammography and sonography in the detection and characterization of primary breast cancer in women at high risk and to delineate the extent of disease in patients with newly diagnosed breast cancer ***(Partridge et al., 2013).***

DWI which is less affected by the state of the background of the mammary gland has sufficient capability of diagnosing non-invasive and invasive breast carcinoma. DWI is different from conventional methods based on blood flow data and has the potential to provide useful information for evaluation of Neoadjuvant chemotherapy ***(Nilsen et al., 2010).***

DWI is a short, non-contrast MRI sequence that has strong potential to increase specificity as an adjunct to conventional breast MRI protocols. DWI measures the apparent diffusion coefficient (ADC), which characterizes the mobility of water molecules in vivo and indirectly reflects tissue cellularity, microstructural characteristics and membrane integrity ***(Khouli et al., 2010).***

Incorporating DWI into conventional breast MRI exams may decrease false positive findings in breast MRI and reduce preventable biopsies ***(Partridge et al., 2009).***

The combination of initial MRI tumor volumetry and final change in MRI volumetry was most predictive of RFS

(recurrence free survival). Longer RFS was observed in the group of patients who had both small initial tumor volume and at least partial volumetric response to chemotherapy ***(Partridge et al., 2009).***

In addition to possible improvement of diagnostic accuracy, MRI has shown superior potential for quantification of tumor size (volumetry) and follow-up after chemotherapy. Objective tumor shrinkage, or tumor response, has been adopted as a standard end point to select new anticancer agents and size is one of the standard prognostic and therapeutic factors in common use today ***(Wu et al., 2012).***

Various breast imaging modalities have been used to detect whether residual malignancy is present or absent after NAC, of which magnetic resonance imaging (MRI) has been increasingly used and recommended in recent years ***(Morrow et al., 2011).***

The accurate assessment of both the response to Neoadjuvant chemotherapy and the extent of residual disease may be crucial to establish further therapeutic plans in patients with locally advanced breast cancer who have received Neoadjuvant chemotherapy ***(Rodenhuis et al., 2010).***

MRI is considered more reliable than other conventional methods of breast cancer imaging such as mammography or breast sonography, for predicting the response to chemotherapy and the extent of residual disease

after Neoadjuvant chemotherapy. MRI has the advantages of providing a three-dimensional image of the breast, with high sensitivity in dense breast tissue, in addition to using non-ionizing radiation ***(Rodenhuis et al., 2010).***

Aim of the Work

The purpose of this study is to evaluate the role of diffusion weighted MRI and volumetry in the assessment of response of breast carcinoma to neoadjuvant chemotherapy.

MRI ANATOMY OF THE BREAST

Normal MRI anatomy of the breast

The anatomy of breast can be demonstrated in details with MRI. Areas of the breast that have been previously beyond the limits of conventional imaging, such as the far posterior breast and chest wall musculature, can be assessed. Normal structures, such as vessels and lymph nodes, are clearly seen particularly with the help of intravenous contrast ***(Morris & Liberman, 2005).***

A good understanding of the structures and normal anatomy of the breast is essential to the proper interpretation of breast MRI ***(Morris & Liberman, 2005).***

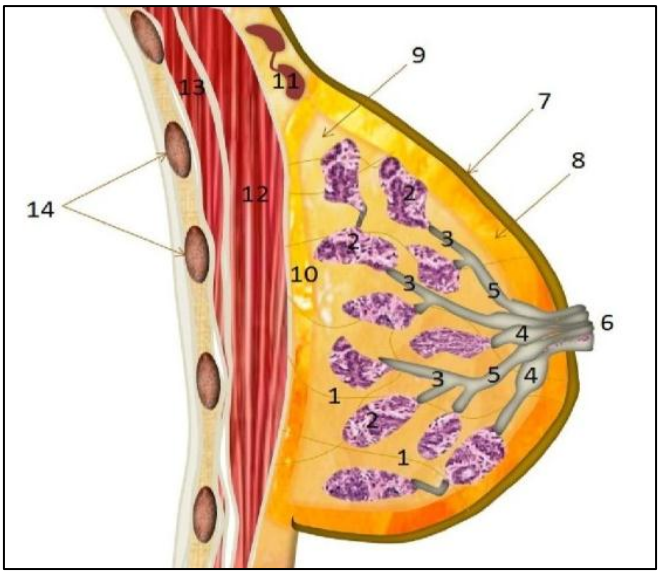

Fig. (1): Represents Breast profile 1- Cooper's ligaments, 2-Breast lobule, 3-Extralobular Duct, 4-Ductal Ampulla (Reservoir), 5- Main Duct, 6- Nipple, 7- skin, 8- Subcutaneous fat, 9- Mammary layer fatty tissue, 10- Retromammary fat, 11- Lymph nodes, 12- Pectoralis Major muscle, 13- Pectoralis Minor muscle ***(Johnson et al, 2010).***

Skin and nipple:

The skin appears smooth and measures usually 0.5 to 2.0mm thick. Skin should not enhance. The nipple-areolar complex enhances intensely and symmetrically on MRI following contrast administration due to the presence of numerous vessels ***(Morris & Liberman, 2005).***

Fascia and chest wall muscles:

The entire breast is enveloped in double layers of superficial pectoral fascia continuous with the superficial abdominal fascia of Camper ***(Morris & Liberman, 2005).***

The undersurface of the breast lies on the deep pectoral fascia covering the pectoralis major and serratus anterior muscles (Fig. 1) ***(Morris & Liberman, 2005).***

Parenchyma and stroma:

The fifth edition of Breast Imaging-Reporting and Data System (BI-RADS) Atlas issued by the American College of Radiology (ACR) included changes in breast density reporting categories as four levels of breast density in keeping with relative increases in the amount of levels of fibro-glandular tissue. These are:- **1. The first 'type' classification** of breast density is of almost entirely fat. Glandular tissue is less than 25%. **2. Type 2** breast density, there is a scattering of fibroglandular tissues, ranging from 25% to 50% of the breast. **3. Type 3** Specialists term the breast tissue in type 3 as 'heterogeneously dense'. The parenchyma ranges from 51% to 75% of the breast tissue. 'Heterogeneous' means something contains many different

items and has many different variations. With respect to breast density, it implies that the fibrous tissue is prevalent throughout the breast, but not clustered together. **Type 4** The highest category of breast density. This means that the breast contains more than 75%glandular and fibrous tissue. At this level the density of the breast may even reduce the sensitivity of the mammogram ***(Perry and Hanson 2014).***

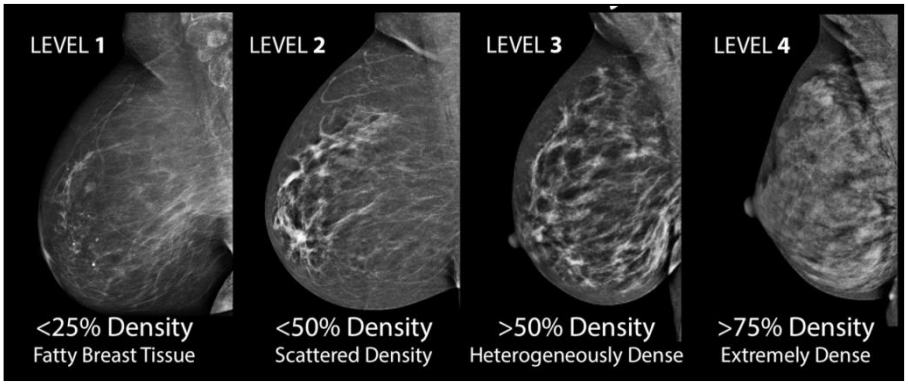

Fig. (2): Represents the different level of breast density as described by the 5th edition of BI-RADS Atlas issued by ACR ***(Gavenonis et al, 2011).***

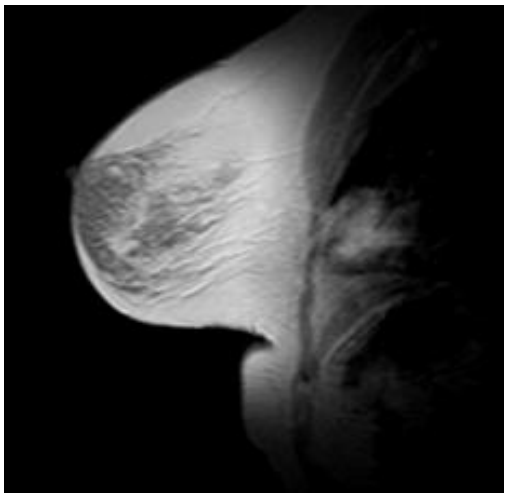

Fig. (3): Sagittal T1-W1 without fat saturation. Breast fat is of high signal intensity, and breast fibro glandular elements appear relatively intermediate to dark ***(Gavenonis et al, 2011).***

Unlike mammography, the dense breasts generally do not present a remarkable difficulty on MRI as contrast is used and thin slices are obtained, thus parenchyma is not a hindrance ***(Kusama et al., 2011)*.**

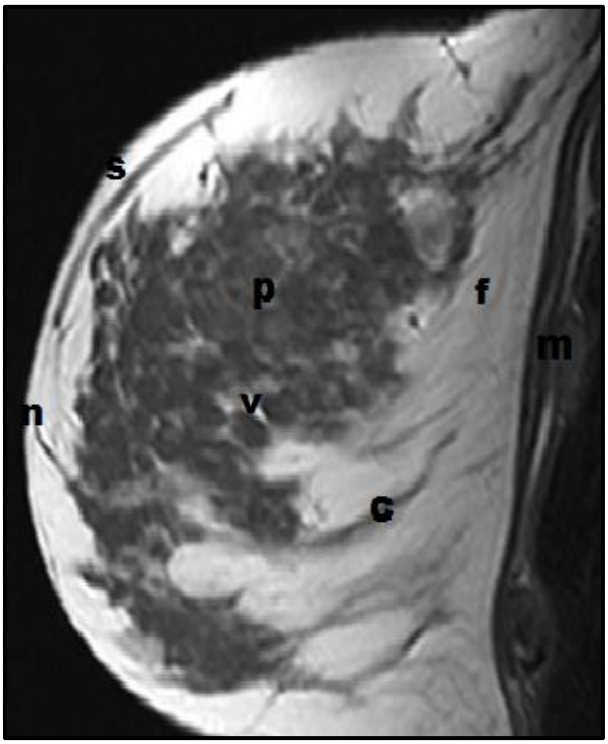

Fig. (4): Sagittal T1-W1 without fat saturation. Breast fat is of high signal intensity, and breast fibro glandular elements appear relatively intermediate to dark. Representative structures are indicated. N, Nipple; S, skin V, vessels; F, fat; p, breast parenchyma (fibro glandular tissue); C, Cooper's ligament; M, pectoralis muscles ***(Gavenonis et al., 2011)***

Blood vessels:

Vessels can be usually differentiated from masses by following the course of the vessel over multiple contiguous sections. Maximum intensity projection (MIP) images can also help to confirm the course of a vessel. Bilateral breast imaging can confirm the impression of benign parenchymal geographic enhancement when the same pattern of enhancement is seen in both breasts ***(Friedman et al., 2009).***

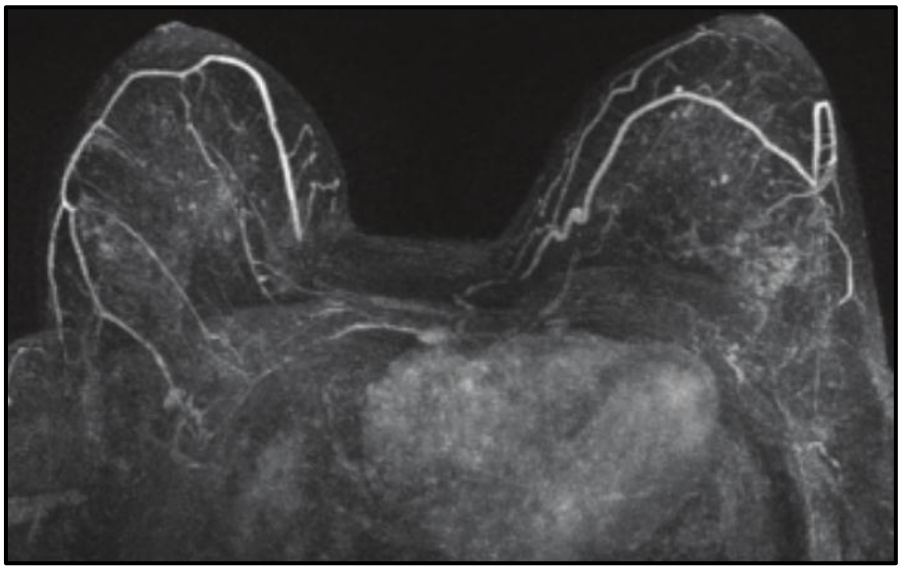

Fig. (5): Axial 3D maximal intensity projection of enhanced breast MRI with fat suppression shows diffuse rather symmetrical enhancement in bilateral breast parenchyma with bilateral vascular enhancement ***(Friedman et al., 2009).***

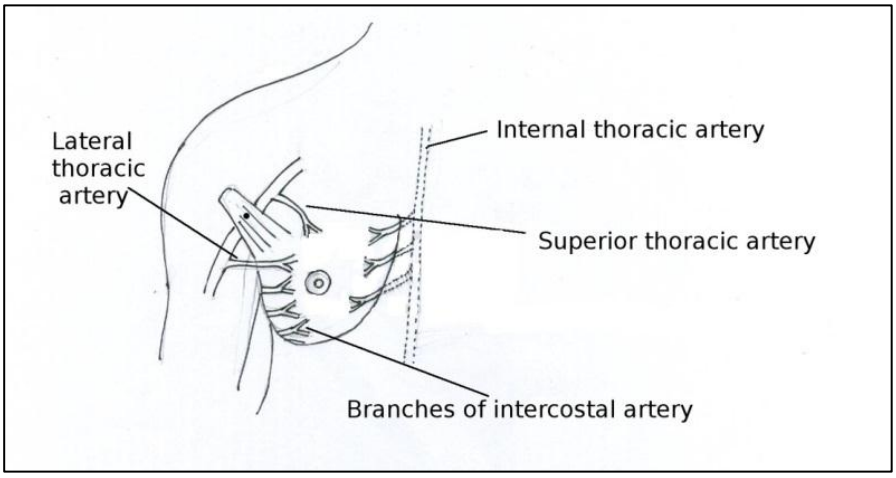

Fig. (6): Blood supply of the breast ***(Johnson et al, 2010)***

Lymph nodes:

As MRI is capable of evaluation more of the posterior breast tissue, and as lymph nodes are highly vascular enhance intensely, it is not surprising that lymph nodes are seen with more frequency on MRI in locations that are considered atypical for mammography. Lymph nodes are easily diagnosed when the characteristic reniform appearance is seen with a fatty hilum ***(Gallardo et al., 2008).***

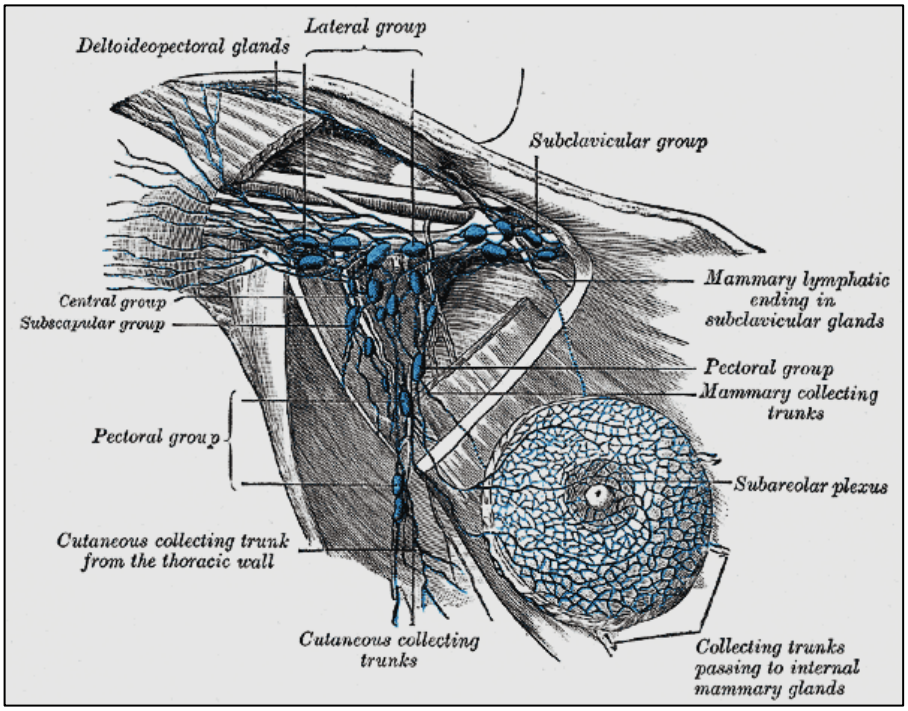

Fig. (7): Lymphatic drainage of the breast ***(Johnson et al, 2010).***

Pathological Aspects of Breast Cancer

Pathology of the breast cancer

Although the majority of breast lumps are benign, nearly one-quarter will be cancerous. Breast cancer is the most frequent cancer in women, where it accounts for 27% of all female cancers. Breast cancer is considered the second after lung cancer as the most prevalent cause of cancer death in women ***(Stanwell and Mountford, 2007).***

There are many types of malignant breast neoplasms which differ in their threat of life. The type, size and extent of spread are vital to predict prognosis and determine the therapeutic approach ***(Lakhani et al., 2005)***

The incidence of breast cancer varies in different breast quadrants. The outer breast quadrants are much more commonly affected than the inner quadrants whereas, about 40% of the cases arising from the upper outer quadrant. In 3% of cases, the disease is diffuse or multifocal. Bilaterality can be noticed in 4% of invasive duct carcinoma and 25% of invasive lobular carcinoma ***(Tavassoli and Devilee, 2003).***

Breast carcinoma includes different histological types. It is customary to divide them into non-invasive (favorable) and invasive categories (Table 1).

Table (1): Histological classification of breast cancer ***(Edge et al., 2010)***

Non Invasive Carcinoma	
DCIS (ductal carcinoma in situ) Includes intracystic & paget's	5%
LCIS (lobular carcinoma in situ)	3%
Invasive Carcinoma	
Duct carcinoma "NOS" (Not Otherwise specified)	72%
Medullary carcinoma	3%
Mucinous carcinoma	2%
Papillary carcinoma	1%
Inflammatory carcinoma	2-4%
Paget's disease	2%
Tubular carcinoma	2%
Lobular carcinoma (Signet-ring cell variant)	10-15%

Non invasive breast carcinoma

Ductal carcinoma in situ (DCIS): Is a unicentric proliferation of epithelial cells with cytological features of malignancy within parenchymal structures of the breast. It is distinguished from invasive carcinoma by the absence of stromal invasion across the basement membrane. Most DCIS is generally considered to arise from the terminal duct lobular units ***(Ellis et al., 2005).***

DCIS is further subdivided into comedo, cribriform, micropapillary, solid and papillary subtypes. Some studies have shown that comedo DCIS (in contrary to other subtypes of DCIS) is associated with many aggressive biologic and clinical features. As a result, further simplification of nomenclature is favored; recognized only comedo and non comedo subtypes ***(Allred et al., 2008).***

Grossly, DCIS appears as a non-capsulated mass with enlarged ducts, many of which contain yellowish necrotic material. On squeezing the mass, necrotic material come out of its cut surface like toothpaste ***(El Sherif et al., 2000).***

Microscopically, these enlarged ducts are lined by several layers of malignant cells without invasion of the basement membrane. This proliferation may assume several patterns including cribriform, papillary and comedo patterns. This comedo pattern is more rapidly followed by infiltration ***(El Sherif et al., 2000).***

Comedo DCIS accounts for 3-5% of all breast carcinomas ***(Allred et al., 2008).*** It is composed of very large pleomorphic cells that have irregular nuclei and abundant eosinophilic cytoplasm, commonly with prominent nucleoli. Comedo carcinoma typically grows in a solid pattern, it often becomes centrally necrotic, and the necrotic debris may undergo dystrophic classification ***(Bartow, 2001).***

As for the non-comedo subtypes; Micropapillary subtype is characterized by small papillary projections of cells without fibro vascular cores while, solid non comedo DCIS is chracterized by uniform cells without discernible acini or micropapillae ***(Allred et al., 2008).***

Noninvasive papillary carcinoma is rare than the other forms of non comedo DCIS. It usually presents as 1-3 cm palpable mass with an intracystic appearance ***(Zhao et al., 2009).***