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Role of Advanced MRI Techniques in Evaluating The Response of Breast Cancer to Neoadjuvant Chemotherapy

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ABSTRACT

Background: Neoadjuvant chemotherapy (NAC) is the favored treatment of choice among locally advanced breast cancer patients because it significantly increases the possibility of breast-conserving surgery. However, for non-responders, an early prediction of response to NAC is essential. Magnetic resonance imaging (MRI) of the breast is an adjunct diagnostic procedure to mammography and ultrasound. Because of its high sensitivity and effectiveness in dense breast tissue, MRI can be a valuable addition to the diagnostic work-up of a patient with breast abnormality or biopsy-proven cancer. **Aim of the Work:** To highlight the role of advanced MRI techniques in the prediction and follow up of the response of breast cancer to neoadjuvant chemotherapy. **Conclusion:** Early change in tumor size measured on MR images is a good predictor of final response after Neoadjuvant chemotherapy (NAC). However, even if the cells respond to treatment, it takes some time for the tumor to shrink. Substantial research effort has been spent on investigating whether other information provided by MR imaging may serve as earlier response indicators than change in tumor size. Techniques that seem to be closest to clinical application, due to their feasibility and the promising results, are the pharmacokinetic analysis of DCE-MRI (Dynamic Contrast Enhanced- MRI), DW-MRI (Diffusion Weighted- MRI) and Spectroscopy.

Keywords: MRI, breast cancer, neoadjuvant chemotherapy.

INTRODUCTION

Neoadjuvant chemotherapy (NAC) is the favored treatment of choice among locally advanced breast cancer patients because it significantly increases the possibility of breast-conserving surgery. However, for non-responders, an early prediction of response to NAC is essential [(1)]. Magnetic resonance imaging (MRI) of the breast is an adjunct diagnostic procedure to mammography and ultrasound. Because of its high sensitivity and effectiveness in dense breast tissue, MRI can be a valuable addition to the diagnostic work-up of a patient with breast abnormality or biopsy-proven cancer [(2)]. Compared with clinical examination, ultrasonography and mammography, dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) is considered the most accurate method for evaluating the extent of residual breast tumor after NAC [(3)].

DW MR imaging without contrast medium may provide diagnostic ability equivalent to that of contrast-enhanced MR imaging in detection of residual breast cancer after neoadjuvant chemotherapy [(4)]. The advantage of DW imaging to help visualize residual breast cancer without the need for contrast medium could be advantageous in women with impaired renal function [(5)].Dynamic contrast agent–enhanced (DCE) magnetic resonance (MR) imaging can depict the distribution of a contrast agent within a tumor over time and noninvasively assess the tissue vasculature. A recent prospective multicenter trial with DCE MR imaging reported that tumor volume measurements were superior to either clinical assessment or diameter measurement in the prediction of pathologic complete response pCR after NAC [(6)]. Another study had previously reported that the initial MR imaging tumor volume and its change after NAC were predictive of recurrence-free survival in breast cancer patients [(7)]. Prediction of response to neoadjuvant chemotherapy with DW MR imaging might help physicians individualize treatments and avoid ineffective chemotherapy [(8)].

Magnetic resonance imaging is the first breast imaging modality that not only allows detailed visualization of the anatomy but also advanced sequences (e.g., diffusion-weighted imaging or spectroscopy) are used, provides functional information [(9)]. There are innovative techniques that go one step beyond morphology and are able to provide a better insight into tumor biology. These techniques are increasingly investigated in clinical trials, but are not yet widely used in clinical routine for breast MRI. Techniques that seem to be closest to clinical application, due to their feasibility and the promising results, are the pharmacokinetic analysis of DCE-MRI (Dynamic Contrast Enhanced- MRI), DW-MRI (Diffusion Weighted- MRI) and Spectroscopy [(10)].

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AIM OF THE WORK

To highlight the role of advanced MRI techniques in the prediction and follow up of the response of breast cancer to neoadjuvant chemotherapy.

The study was done after approval of ethical board of Ain Shams university.

ANATOMY OF THE BREAST

EMBRYOLOGY

Breast arises from a single ectodermal bud. At the fifth to sixth week of fetal life a milk streak develops as an ectodermal thickening extending from the axilla to the pelvis known as galactic band **(figure 1**). By the ninth week most of this has atrophied except for a mammary ridge in the pectoral region. There is a mass of basal cells proliferates to form the nipple bud. By the 12th week squamous cells from the surface begin to invade the nipple bud while the epithelial cells grow downward as mammary ducts terminating in lobular buds. The mesenchymal cells differentiate into smooth muscles of the nipple and areola. The anlage of the lactiferous ducts invades the mesodermal connective tissue by 16 to 24 week.

During the second trimester, the breast continues to develop with the appearance of sweat glands, sebaceous glands and apocrine glands which will develop into the montegomery glands around the nipple. During the final weeks of development the mammary gland mass increase fourfold and the nipple areolar- complex develops and become pigmented. Shortly after birth there is withdrawal of the placental hormones causing cholesterol secretion to stop and involution of the breast [(11)].

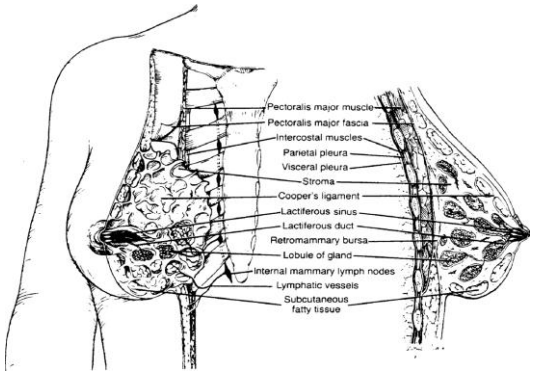


Figure (2): Anatomical structures of the breast and underlying chest wall [(14)].

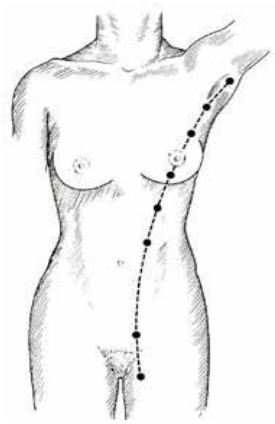


Figure (1): The extent of mammary ridge [(12)].

GROSS ANATOMY

The adult breast lies between the second and sixth ribs in the vertical axis and between the sternal edge and the midaxillary line in the horizontal axis ***(Figure 2).*** The average breast measures 10 to 12 cm in diameter, and its average thickness centrally is 5 to 7 cm. Breast tissue also projects into the axilla as the axillary tail of Spence. The superficial pectoral fascia envelops the breast and is continuous with the superficial abdominal fascia of Camper. The undersurface of the breast lies on the deep pectoral fascia, covering the pectoralis major and anterior serratus muscles. Connecting these two fascial layers are fibrous bands (Cooper suspensory ligaments) that represent the "natural" means of support of the breast. The contour of the breast varies but is usually dome-like, with a conical configuration in the nulliparous woman and a pendulous contour in the parous woman [(13)].

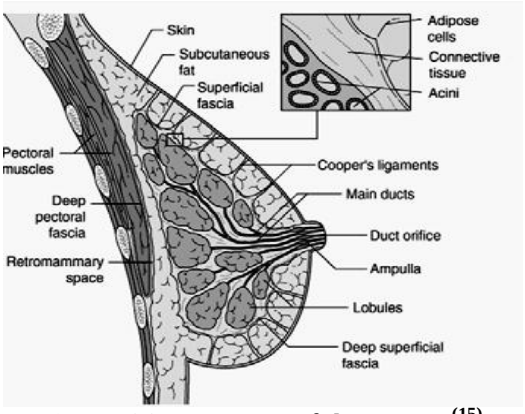


Figure (3): Anatomy of the Breast [(15)].

MRI anatomy of the female breast

MRI provides a sectional image of the breast with good visualization of its different components (glandular tissue, fat, skin and nipple).

It can show the relationship of breast tissue to the surrounding Structures, demonstrate the distribution of fibroglandular tissue and fat, and accurately assess the volume of dense tissue [(16)].

Skin and nipple

The skin appears smooth and measures usually 0.5-to 2.0-mm 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 ***(Figure 4)*** [(2)].

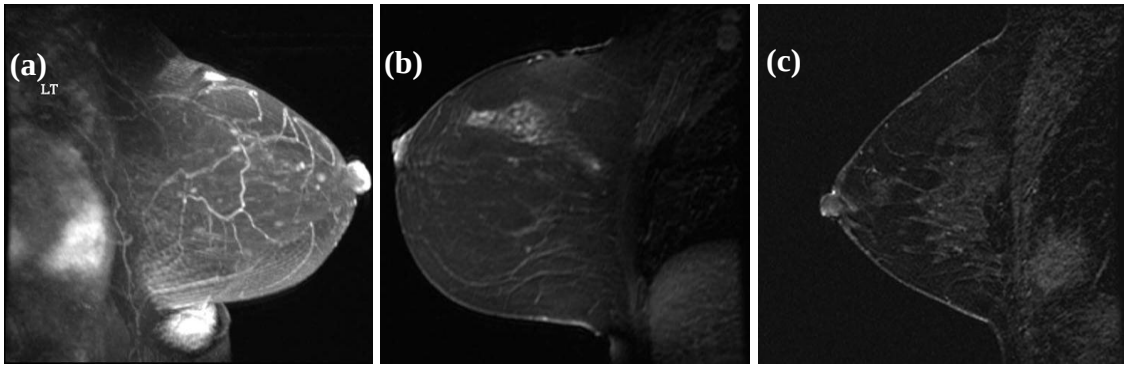


Figure (4): Nipples on MRI may (A) enhance intensely, (B) mildly, or (C) not at all, depending on blood supply [(2)].

PATHOLOGY OF CANCER BREAST

Epidemiology

Breast cancer is the second leading cause of deaths in women today and it is the most common cancer among women worldwide (23%of all new cancer cases) [(17)]. The median age is 50 years and the majority is postmenopausal. Female to male incidence is 50: 1 [(18)].

Breast Cancer in Egypt

In Egypt, breast cancer is the most common cancer among women, representing18.9% of total cancer cases (35.1% in women) among the **Egypt National Cancer Institute (NCI)** [(19)] series of 10556 patients during the year 2001 [(20)]. Breast cancer in Egyptian patients is a biologically more aggressive disease than that encountered in the west. This is explained partly by the late presentation of patients at an advanced stage [(21)].

Pathogenesis

The pathogenesis of breast cancer is poorly understood, but epidemiologic, molecular, and genetic studies outline complex risk factors. Breast cancers also exhibit diversity in histopathology, molecular features, and overall patient outcomes. Hence the disease can be viewed as a multifaceted and complex epithelial malignancy. Approximately 5% of breast cancers are thought to reflect a hereditary predisposition. Carcinoma in situ of the breast refers to the presence of apparently malignant epithelial cells that have not penetrated the basement membrane [(22)]. Cancer can occur anywhere within the breast perimeter, including in supernumerary breast tissue. Most breast cancers occur in the upper outer quadrant and sub areolar region because that is where most of the tissue is located [(23)].

Risk factors of breast cancer

The risk factors associated with breast cancer are complex and include demographic, genetic, biologic, reproductive, hormonal, and environmental factors. Age, gender, and family history are among the strongest risk factors for breast cancer, although it is well known that serum levels of endogenous sex hormones are also strongly associated with an increased risk of breast cancer [(24)].

Table (1): Risk factors for breast cancer: [25].

Risk Factors	Estimated Relative Risk
Advanced age	**More than 4**
Family history	
Family history of ovarian cancer in female less than 50y old	**More than 5**
One first degree relative (mother, sister)	**2**
Two or more relatives	**2**
Personal history	
Personal history	**3-4**
Positive BRCA1/BRCA2 mutations	**More than 4**
Breast biopsy with atypical hyperplasia	**4-5**
Breast biopsy with DCIS or LCIS	**8-10**
Reproductive history	
Early age at menarche (less than 12 y)	**2**
Late age of menopause	**1.5-2**
Increased age at full term pregnancy (more than 30 y)/nulliparity	**2**
Current or recent use of oral contraceptives	**1.5-2**
Use of combined estrogen/progesterone HRT	**1.25**
Life style factors	
Sedentary life	**1.5-2**
Adult weight gain	**1.3-1.5**
Alcohol consumption	**1.5**

Histo-pathological Classification of malignant breast lesions:

The vast majority (>95%) of breast cancers arise from epithelial cells **(Figure 5),** that are found in the terminal duct lobular unit, and are, therefore, classified as carcinomas. These carcinomas can be divided into two distinct groups: (1) In situ carcinomas—where cancer cells remain within the basement membrane of the elements of the terminal duct lobular unit and the draining duct; and (2) Invasive or infiltrating carcinomas—where there is dissemination of cancer cells outside the basement membrane of the ducts and lobules and invasion of the breast stroma and consequently have the potential to metastasize. Both in situ and invasive cancers have characteristic patterns by which they can be classified [26].

There are two major histologic types of in situ carcinoma, referred to as ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). There are several different histologic types of invasive breast cancer, including invasive ductal carcinoma (IDC) not otherwise specified, invasive lobular carcinoma (ILC), mixed ductal/lobular carcinoma, mucinous (colloid) carcinoma, tubular carcinoma, medullary carcinoma, and papillary carcinoma. IDC is the most common histologic subtype, accounting for approximately 75% of all invasive breast cancers [27].

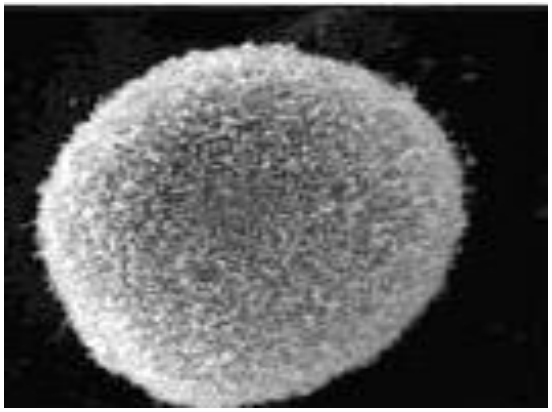


Figure (5): Breast cancer cell, showed by a scanning electron microscope [28].

Non-epithelial breast malignancies include primary lymphomas, sarcomas, haematological malignancies, melanomas as well as secondary metastases to the breast. They account for less than 1% of all breast tumors [29].

TECHNIQUE OF ADVANCED MRI IMAGING OF THE BREAST

Introduction to conventional MRI

Magnetic resonance imaging is the first breast imaging modality that not only allows detailed visualization of the anatomy but also, when an intravenous contrast agent is administered or advanced sequences (e.g., diffusion-weighted imaging or spectroscopy) are used, provides functional information [9].

Magnetic resonance imaging (MRI) of the breast is an adjunct diagnostic procedure to

mammography and ultrasound. Because of its high sensitivity and effectiveness in dense breast tissue, MRI can be a valuable addition to the diagnostic work-up of a patient with breast abnormality or biopsy-proven cancer [(2)].

Advanced MRI techniques

A- Dynamic contrast enhanced MRI (DCI-MRI)

The most commonly used sequence in breast MRI is a T1-weighted, dynamic contrast enhanced acquisition. The sequence is called 'dynamic' because it is first performed before contrast administration and is repeated multiple times after contrast administration [(30)].

1- Magnetic field strength

Increasing field strength (1.5 T, 3T) allows a higher spatial resolution at a similar temporal resolution and consequently may increase diagnostic confidence [(31)].

2- Shimming

It is used to reduce magnetic field in homogeneities across the volume of the FOV [(5)].

3-Breast Coils

A dedicated bilateral breast coil *(Figure 6)* is mandatory for this investigation [(30)]. Multichannel coils provide a higher signal to noise ratio (SNR) and more uniform image intensity across both breasts. Both the 4-channel bilateral breast coil and the newer 7- and 12-channel bilateral coils are compatible with current parallel imaging techniques [(32)].

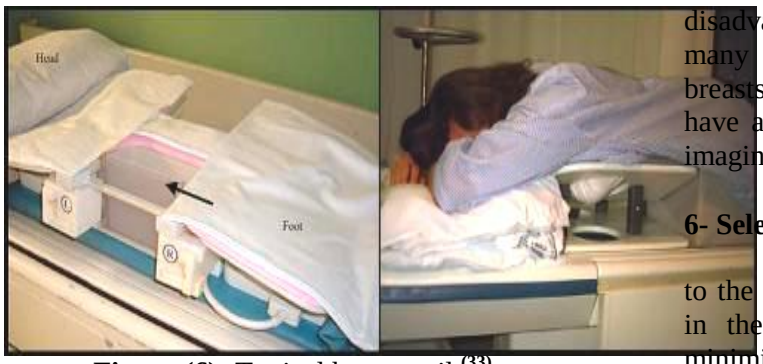


Figure (6): Typical breast coil [(33)].

4- Sequences

Various MR imaging protocols may be used to obtain breast images of acceptable quality. A standard protocol includes:

a) T2-weighted rapid (fast or turbo) spin-echo (repetition time msec/echo time msec, 4000/90; section thickness, ≤4 mm) acquisition can be performed as a start [(34)].

b) Three-dimensional T1-weighted gradient echo (GE) (20/4.5; flip angle, 30°–45°; section thickness, ≤3 mm) acquisitions [(34)].

T1-weighted 3D or 2D (multi-slice) spoiled gradient echo pulse sequence is obtained before contrast injection and then repeated as rapidly as possible for 5 to 7 min after a rapid intravenous bolus of a Gd-containing contrast agent [(30)].

A 3D pulse sequence offers a stronger T1 contrast and enables thinner slices than 2D; in turn, a 2D sequence suffers less motion and pulsation artifacts. Both sequences can be performed with and without fat suppression [(30)].

5- Orientation of image acquisition

The choice of the image orientation is important. For bilateral dynamic breast MRI, axial or coronal orientations are most frequently used. Coronal imaging has advantages in that it can reduce heart pulsation artifacts, but it is more susceptible to respiration motion and also to flow artifacts because vessels tend to travel perpendicular to the slice encoding direction [(30)].

The sagittal plane is probably the most natural way to image the breast. The technical advantage of the sagittal plane is that a relatively small field of view (FOV) will be sufficient to cover the breast, which will improve the spatial resolution at a given acquisition matrix. The only disadvantage of the sagittal plane is that far too many sections would be needed to cover both breasts. Accordingly, sagittal imaging protocols have almost always been used for single breast imaging [(28)].

6- Selection of the Phase-encoding Direction

Cardiac and respiratory motion may lead to the propagation of artifacts across the breasts in the in-plane phase-encoding direction. To minimize such effects, the in-plane phase-encoding direction should never be anterior-posterior *(Figure 7).* For sagittal and coronal imaging, the phase-encoding direction should be superior-inferior. For axial imaging, the phase-encoding direction should be left-right [(32)].

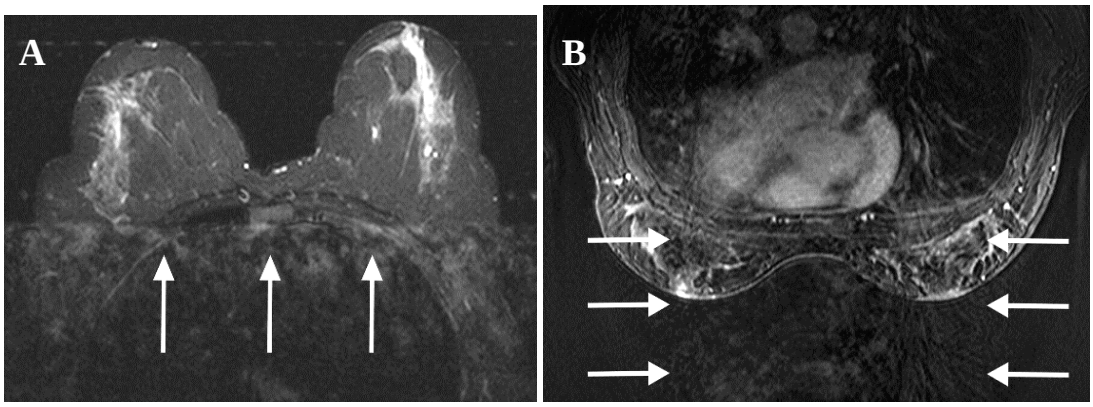


Figure (7): (a) Axial contrast-enhanced T1- MRI acquired with improper selection of the anterior-posterior direction showing cardiac motion–related artifact propagated across the breasts in a vertical direction (arrows). **(b)** Axial T1-weighted image acquired in another patient with the left-right direction (arrows) providing better depiction of the breasts [(32)].

7- Adequate temporal resolution

The required temporal resolution is determined by the time course of contrast agent uptake. Peak contrast enhancement in a malignant lesion typically occurs between 90 and 180 seconds after injection of the contrast agent, so a temporal resolution of less than 2 minutes is crucial for accurate depiction of the kinetics of lesion contrast enhancement [(32)].

Signal intensity curve (**Figure 8)**

- Continuous or persistent (type 1) — a pattern of progressive enhancement, with continuous increase in signal intensity. This is also coincides with delayed enhancement phase that refers to the signal intensity curve after 2 minutes or after curve starts to change. This shape is typically seen in benign lesions.
- Plateau (type 2) — initial increase in signal intensity followed by a flattening. This type of enhancement can be found in benign and malignant lesions.
- Washout (type 3) — an initial increase and subsequent decrease in signal intensity; malignant lesions typically show this type of dynamic pattern [(35)].

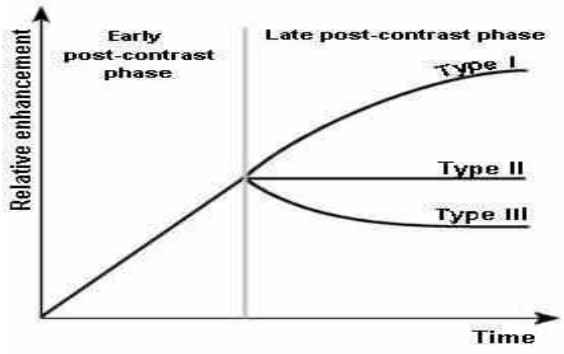


Figure (8): Time intensity curve.On the *x*-axis the time in minutes is shown, on the *y*-axis the relative increase of signal intensity in percent [(35)].

Evaluations of the response of breast cancer to neoadjuvant chemotherapy using advanced MRI techniques

Neoadjuvant Chemotherapy

Chemotherapy uses drugs to destroy cancer cells, stop their growth, or ameliorate symptoms. In neoadjuvant (also called preoperative or primary) chemotherapy, drug treatment takes place before surgical extraction of a tumor. Oncologists administer neoadjuvant therapy with the objective of reducing tumor size [(35)]. Reduction of tumor mass decreases the extent and invasiveness of a surgery and makes it easier for the surgeon to distinguish between normal and cancerous tissue. In tumors initially diagnosed as non-operable or of borderline respectability, shrinking of the cancerous lesion can enable surgery and allow for adequate clean margins. The neoadjuvant chemotherapy not only facilitates the procedure but can also improve postoperative recovery and the long-term outcome for the patient [(36)].

Neoadjuvant chemotherapy is usually given for inoperable breast cancers and it is a treatment option for many other solid tumors. Systemic preoperative treatment is employed in breast-conserving surgery, tumors with borderline resectability and locally advanced cancers [(37)].

The administration of neoadjuvant chemotherapy is performed in cycles, with each cycle consisting of a treatment period followed by a resting phase. Chemotherapy agents can be given orally or intravenously during a variable number of cycles14-16. Response to chemotherapy and patient fitness are important criteria in determining patient eligibility for surgery 17. In some patients, surgery can be

performed only weeks after the last cycle of preoperative chemotherapy [38].

Tumor response may be assessed readily by the use of Response Evaluation Criteria in Solid Tumor version 1.1. However, the criteria mainly depend on tumor size changes. These criteria do not reflect other morphologic (tumor necrosis, hemorrhage, and cavitation), functional, or metabolic changes that may occur with targeted chemotherapy or even with conventional chemotherapy. The state-of-the-art multidetector CT is still playing an important role, by showing high-quality, high-resolution images that are appropriate enough to measure tumor size and its changes. Additional imaging biomarker devices such as dual energy CT, positron emission tomography, MRI including diffusion-weighted MRI shall be more frequently used for tumor response evaluation, because they provide detailed anatomic, and functional or metabolic change information during tumor treatment, particularly during targeted chemotherapy [39].

Based on clinical and imaging findings, using the measurements have obtained with PE and MRI and according to the "Response Evaluation Criteria in Solid Tumors (RECIST)", the responses to chemotherapy have classified into the following categories [40]**:**

1- Responders:

-Complete Response (CR): no clinical evidence of residual tumor

-Partial Response (PR): reduction in size of the tumor more than 30%

2- No Responders:

-Stable Disease (SD): reduction in size of the tumor inferior than 30%

- Progressive Disease (PD): increase in size of tumor or presence of new lesions

Advanced MRI breast techniques (functional MRI):

Early change in tumor size measured on MR images is a good predictor of final response after Neoadjuvant chemotherapy (NAC). However, even if the cells respond to treatment, it takes some time for the tumor to shrink. Substantial research effort has been spent on investigating whether other information provided by MR imaging may serve as earlier response indicators than change in tumor size. Techniques that seem to be closest to clinical application, due to their feasibility and the promising results, are the pharmacokinetic analysis of DCE-MRI (Dynamic Contrast Enhanced- MRI), DW-MRI (Diffusion Weighted- MRI) and Spectroscopy [10].

Dynamic contrast-enhanced MRI (DCE-MRI)

Contrast enhanced MRI is valuable for diagnosis of small tumors in dense breast with the structural and kinetic parameters improved the specificity of diagnosing benign from malignant lesions. It is a complimentary modality for preoperative staging, to follow response to therapy, to detect recurrences and for screening high risk women [41].

Pharmacokinetic assessment in the dynamic contrast-enhanced MRI (DCE-MRI) Technique

The determination of residual tumor size is underestimated and unreliable in carcinomas significantly responding to chemotherapy which may lead to missed detections in up to 30% of patients. There is now increasing evidence that functional analysis of the microcirculation by using dynamic contrast material-enhanced MR imaging could be used to identify responders and non-responders during and/or after neoadjuvant chemotherapy more reliably than conventional anatomic MRI results alone [42].

A simplified pharmacokinetic assessment in routine DCE MRI of the breast can be done by evaluating the signal intensity curve. The greatest mean maximum percentage enhanced area in the tumor was chosen to be region of interest (ROI). The types of curves were classified to be I type (gradual enhanced), II type (plateau enhanced) and III type (wash-out enhanced) *(Figure 9)* [43].

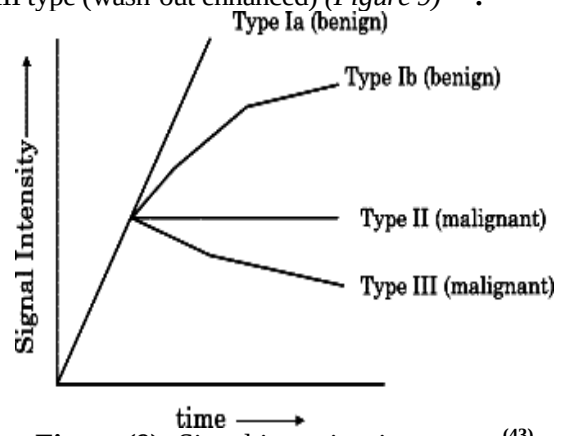


Figure (9): Signal intensity-time curve [43]

For pharmacokinetic analysis, commercially available software is used. Within this software, ROIs can be manually drawn over the tumour volume on subtracted images and then copied on pixel-by-pixel colour maps, representing on a colour scale each pixel value for the following pharmacokinetic parameters (quantitative perfusion parameters) *(Figure 10)* [44].

-**K trans** measures the leakage of contrast agent into the extravascular-extracellular space

-**K ep** measures the back flux of contrast agent from extravascular-extracellular space into the vascular space
-**V e** measures the fraction of volume where contrast agent can leak into the extravascular-extracellular space
-**i AUC 60** measure the integral of the area under the concentration-time curve up to 60 s

The values of the pharmacokinetic parameters for the selected ROI can be expressed in summary statistics (mean, median and standard deviation) or in histograms [44].

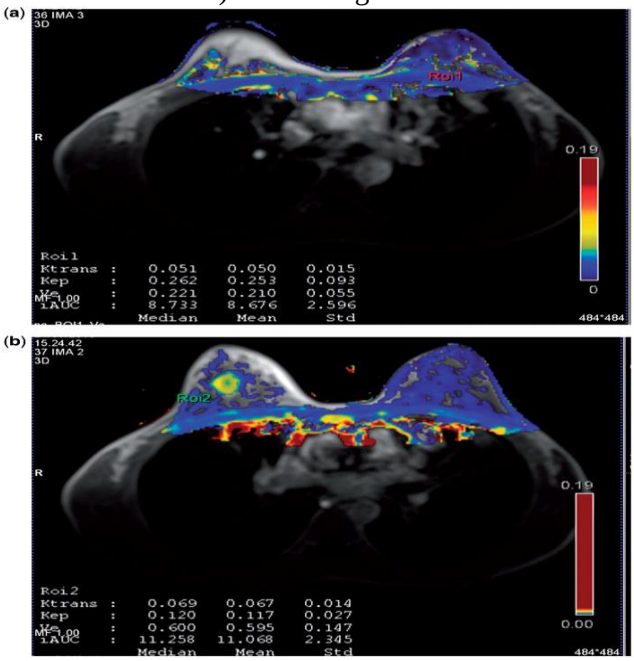


Figure 10: Pixel-by-pixel colour maps with each pixel representing values for K trans (other maps can be generated for K ep, Ve, iAUC60). The tabulated values are derived from the ROIs drawn on subtracted images and copied to the colour maps for each parameter. In this example, ROI 1 is for breast cancer (a) and ROI 2 is for fibroadenoma (b) [44].

Clinical applications

The pharmacokinetic parameters might serve as a surrogate biomarker of angiogenesis. Previous articles have shown a correlation between contrast enhancement and micro vessel density (MVD). These parameters have different values in tumours due to the process of neoplastic angiogenesis. In particular, K trans values are expected to be higher in breast cancer than in benign lesions and in normal breast tissue due to the higher presence of leaky capillaries in breast cancer. Similarly K ep is also expected to be higher in breast cancer, because it is another measure of capillary leakiness. i AUC 60 is also expected to be higher in breast cancer due to the greater contrast uptake in breast cancer. In contrast, V e is expected to be lower in tumours, due to a smaller extravascular-extracellular space, as a result of higher cellularity and vascularity in tumors [44].

In another study the following different pharmacokinetic parameters evaluating hot spots and also cold spots inside a tumour were calculated according to the equations shown in *(Table 8).*

Table 8: Calculation methods for magnetic resonance enhancement patterns [45]

Parameter	Calculation	Definition
E n	En= (SI n – SI base) / SI base	Relative improvement in SI at each postcontrast measurement compared with the precontrast phase
Slope in	Slope in = E peak / T peak	Rate of change of contrast enhancement from the precontrast phase up to the peak
Washout	Washout = (SI peak –SI 12) / SI 12[a]	Relative decrease in maximal SI compared with the last postcontrast phase
Abbreviations: En=enhancement ratio; E peak=peak En; n=1-12; ROI=region of interest; SI=signal intensity; SI base= precontrast SI; slope in=inflow slope; Tpeak =time elapsed between the administration of contrast agent and the phase at which the maximal SI value was obtained. a For a "truly poorly" enhancing cold-spot ROI, which might never reach peak enhancement, SI peak was equal to SI 12.		

Slope in was used to indicate the inflow velocity of contrast material, and washout was used to indicate the outflow velocity of contrast material, cold spot parameters, hot spot parameters, and heterogeneity parameters were calculated as follows:

1. **Cold-spot parameters**: slope C = inflow slope at the cold spot; Washout C = washout slope at the cold spot
2. **Hot-spot parameters:** slope H =inflow slope at the hot spot; Washout H = washout slope at the hot spot.
3. **Heterogeneity parameters**: ratio-in =inflow slope ratio =slope H/slope C; ratio-out = washout slope ratio = (washout H– washout C)/washout H; washout D= absolute difference in washout rates = washout H – washout C.

The hot-spot parameters indicated the regions with a sufficient blood supply, whereas cold-spot parameters indicated the regions with ischemia. The heterogeneity parameters may, to some extent, reflect tumor heterogeneity [(45)].

Role of pharmacokinetic parameters in evaluation of response

General response assessments of breast cancer to neoadjuvant chemotherapy are based on several factors:

1. Residual tumour size

On RECIST (Response Evaluation Criteria in Solid Tumors) criterion, therapy responses were evaluated by measuring the maximum diameter of tumor (measured on the 90-120 second subtraction image). This is also a conventional method to make response assessments of solid tumors. Present researches indicated that it will be more effective if we used 3D volume change to make the assessments, especially for irregular or multifocal lesions [(43)].

3D MIP is used to calculate tumor extent from different angles, so that small residual lesions can be assessed. Volume calculations are derived from the post-contrasted sequence. ROIs are drawn around all areas of tumour on subtracted slices. The area of the pixels within all the ROIs are then summated and multiplied by 3D MIP (maximum intensity projection) to give the overall tumour volume [(43)].Previous studies showed that tumor volumes didn't change significantly after 1st cycle of NAC whether in responders or non-responders. Therefore, tumor volume didn't change much enough to be detected by radiologic examinations at early phase of NAC. Patient's with a < 65% reduction in total tumour volume was categorized as "non-responders", while with a ≥ 65% reduction was categorized as "responders" [(43)].

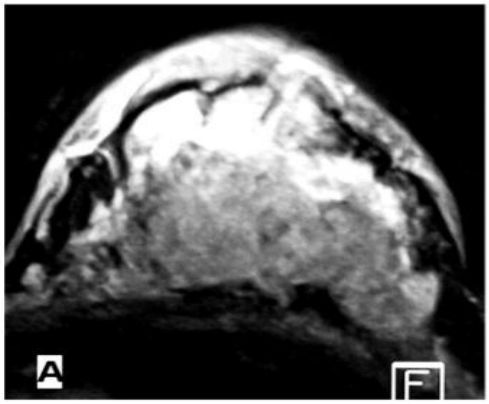
2. Change of tumor morphology

Shrinkage pattern was classified by Zhang et al., [(44)] into concentric shrinkage and dendritic shrinkage pattern. In concentric shrinkage pattern, tumor shrinks to the centre, and to be isolated node finally *(Figure 11).* Whereas, in dendritic shrinkage pattern, tumor shrinks to be dendritic or multifocal lesions finally *(Figure 12).* Residual lesions with concentric shrinkage were easily to evaluate the extent, so that breast conserving surgery can be considered. While after tumor excision of tumors with dendritic shrinkage pattern, positive margins are always found, so that only radical mastectomy can be considered. Therefore, accurate assessment of tumor shrinkage pattern will aid to choose reasonable surgery strategy ***(Wang et al., 2010).***

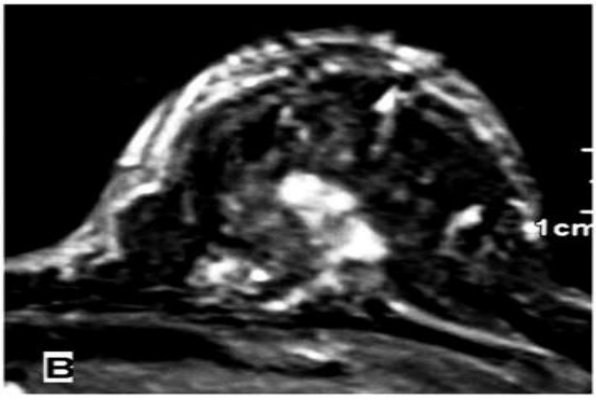
ILLUSTRATIVE CASES

CASE 1

History: 42 year old Female presented with left breast lump



A. Contrast-enhanced MRI before chemotherapy shows a 7-cm irregular mass in upper part of the breast.



B. After completion of chemotherapy CE-MRI shows a 1.5 cm area of regional enhancement at the site of previous tumor there was Partial Response (PR).

Figure (11)

CASE 2

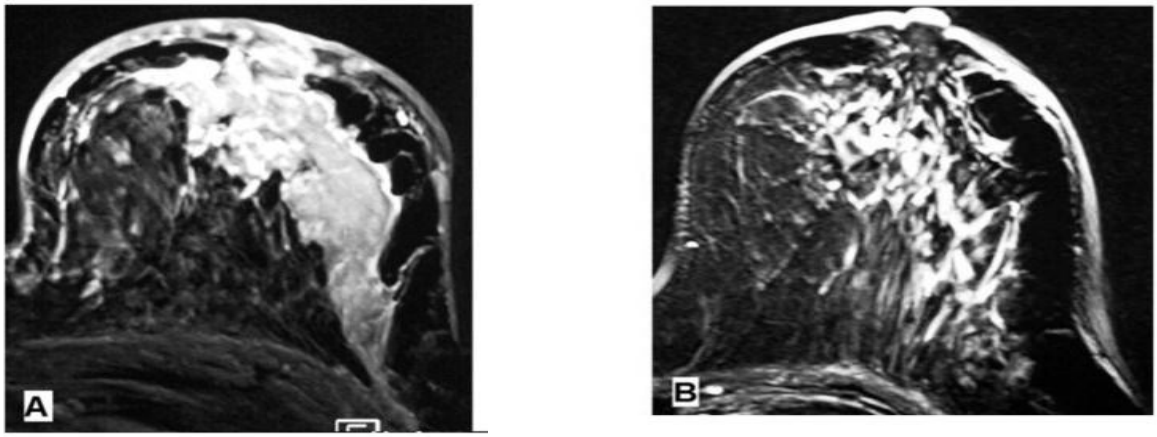


Figure (12)

A. Contrast-enhanced T1-weighted MRI before chemotherapy shows a 8-cm area of regional enhancement at the central and lateral portion of the left breast.

B. After completion of chemotherapy at CE-MRI there is no visible abnormal enhancement there was Complete Response (CR): no clinical evidence of residual tumor.

HISTORY

48 year old Female presented with left breast lump.

CONCLUSION

Early change in tumor size measured on MR images is a good predictor of final response after Neoadjuvant chemotherapy (NAC). Techniques that seem to be closest to clinical application, due to their feasibility and the promising results, are the pharmacokinetic analysis of DCE-MRI (Dynamic Contrast Enhanced-MRI), DW-MRI (Diffusion Weighted- MRI) and Spectroscopy.

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