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THE DIFFUSION -WEIGHTED IMAGES WITH CONVENTIONAL BREAST MRI IN DETECTION AND DIFFERENTIATION OF BREAST LESION

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ABSTRACT

Contrast enhanced MR imaging of the breast is sensitive for detection of invasive breast cancer, DWI represents an easy breast imaging sequence providing valuable information on benign and malignant lesions by DETECTION tumor. DWI has shown high sensitivity for breast cancer thus recommended as a part of routine preoperative examination.

INTRODUCTION

Benign lesions of the breast are more frequent than malignant ones. It is important to recognize benign lesions and distinguish them from breast cancer.(*Guray and sahin,2006*) increasing rate of breast cancer continues to be a major area of concern for both clinicians and researchers. Increased awareness in the affected population leads to more frequent physical examinations and diagnostic imaging procedures which results in earlier diagnosis and hence improved prognosis. *(Guo et al, 2002*)

Mammography has been proven to detect breast cancer at an early stage, other screening technologies also may contribute to the earlier detection of breast cancer, particularly in women under the age of 40 years for whom mammography is less sensitive such as breast ultrasound or magnetic resonance imaging [MRI]). *(Saslow et al,2007)*

Breast MRI has become an important tool for breast cancer detection and characterization. Dynamic contrast-enhanced MRI is highly sensitive for breast cancer, allowing detection of malignancy that is occult on physical examination, mammography, and sonography. *(Wang et al, 2009)*

Breast MRI may be used to distinguish between benign and malignant LESION, this may reduce the number of breast biopsies done to evaluate a suspicious breast mass. Although MRI can detect tumors in dense breast tissue, it cannot detect tiny specks of calcium (known as micro calcifications), which account for half of the cancers detected by mammography. *(Wax, 2009)*

Breast MRI exams involve a contrast-enhanced scan to highlight tissue with increased vascularity, very sensitive for detecting malignancies but also producing many false-positives. Diffusion tensor imaging (DTI) is a different type of MRI that measures the mobility of water in tissue. DTI is sensitive to characteristics often disrupted in malignant breast tissues, such as cell organization, density, extracellular space, and cell membrane permeability, which may help to better discriminate between different types of breast lesions. *(Partridge et al, 2007)*

Tumor response has been assessed via tumor size measurements during the course of a treatment. an earlier assessment of treatment to facilitate early cessation and cost savings. Diffusion-weighted imaging (DWI) has been identified by preclinical studies to be a likely alternative to tumor size measurements. *(Pickles et al, 2006)*

Using Diffusion-weighted imaging (DWI) combined to MRI is helpful to distinguish malignant versus benign breast lesions and it also may reduce the number of unnecessary breast biopsies. *(Barker and Salkowski, 2009)*

Anatomy of the Breast

The breasts form a secondary sexual feature of females also present in a rudimentary form in males. The breasts are the site of malignant change in as many as one in ten women. *(Ellies etal, 1993)*

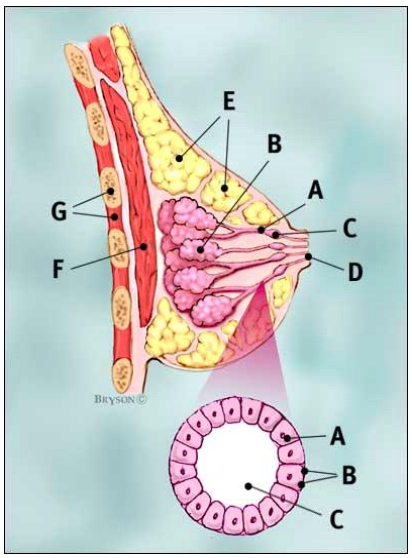
In the female they are two large hemispherical eminences lying within the superficial fascia and situated on the front and sides of the chest, each extends from the

second rib above to the sixth rib below and from the side of the sternum to near the mid axillary line. *(Hansen et al, 2005)*

The breast lies on the deep pectoral fascia, the superficial pectoral fascia envelops the breast, suspensory ligaments called Cooper's ligaments connect the two layers providing a degree of support to the breast and giving the breast its shape. *(Jonathan et al., 2008)*

The breast has no muscle tissue. A layer of fat surrounds the glands and extends throughout the breast. *(Ellies et al, 1993)*

Each breast contains 15 to 20 lobes arranged in a circular fashion. The fat (subcutaneous adipose tissue) that covers the lobes gives the breast its size and shape. Each lobe consists of smaller lobules that make up even smaller bulbs referred to as a terminal ductal lobular unit(TDLU). The TDLU consists of the intralobular duct along whose lumen and end protrude blunt or round saccules called ductules, which differentiate into the secretory units or acini during lactation. The TDLUs are embedded in specialized, hormonally responsive connective tissue stroma, the intralobular stroma. This network of lobes, lobules and bulbs are all interconnected and end at the nipple. Ducts connect the lobes, lobules, and glands. In nursing mothers these ducts deliver milk to openings in the nipple (fig 1). The areola is the darker-pigmented area around the nipple. *(Gray, 1989)*



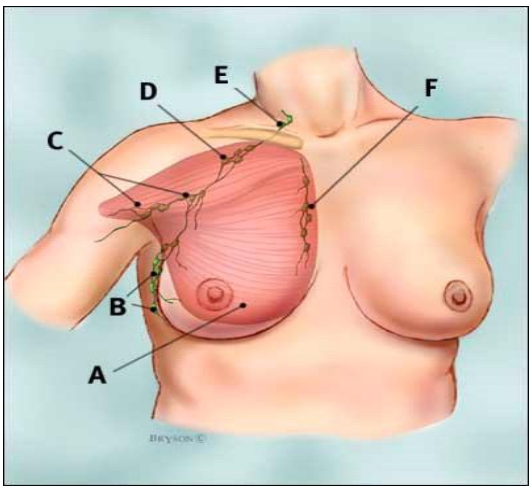
A Ducts
B Lobules
C Dilated section of duct to hold milk
D Nipple
E Fat
F Pectoralis major muscle
G Chest wall/rib cage

Enlargement
A Normal duct cells
B Basement membrane
C Lumen (center of duct)

(Ellies et al, 1993)
Arterial supply
The medial part of the breast is supplied by perforating branches of the internal mammary artery and by intercostal arteries. The lateral part is supplied by branches of the axillary artery, namely: the external mammary, the subscapular and branches from thoraco-acromial artery**. *(Omar, 2001)***

Venous drainage
Venous drainage usually corresponds to the arteries listed previously. However the veins of the breast, as the veins elsewhere, may show wide variations. ***(Ellis et al, 1993)***

Lymphatic drainage: (fig.2)
The breast is drained by lymph nodes to multiple areas that include the skin surrounding the breast, the chest wall, and the axilla. The majority of the lymphatic drainage is via the axilla region. This is why general surgeons use the lymph nodes in the axillary region to assess the spread of breast cancer when considering the appropriate therapy. ***(Ellis et al, 1993)***



A Pectoralis major muscle
B Axillary lymph nodes: level I
C Axillary lymph nodes: level II
D Axillary lymph nodes: level III
E Supraclavicular lymph nodes
F Internal mammary lymph nodes

(Ellies et al, 1993)
A-Classifications of benign breast diseases
A-Common Benign Breast Lesions
Developmental abnormalities
Ectopic breast (mammary heterotopia): is described as supernumerary and aberrant breast tissue,it is the most common congenital abnormality of the breast. Supernumerary breast tissue is seen mostly along the

milk line; the most frequent sites are the chest wall, vulva, and axilla,while Aberrant breast tissue is usually located near the breast, most commonly in the axilla and usually have a nipple and areola and a separate duct system from that of the normal breast.*(Guray and Sahin,2006).*

*Underdevelopment of the breast (hypoplasia):*when congenital, is usually associated with genetic disorders.Acquired hypoplasia, on the other hand, is usually iatrogenic, most commonly subsequent to trauma or radio-therapy. The complete absence of both breast and nipple or presence of only nipple without breast tissue is rare. *(Guray and Sahin,2006)*

Inflammatory and related lesions

Mastitis

A variety of inflammatory and reactive changes can be seen in the breast. While some of these changes are a result of infectious agents, others do not have a well-understood etiology and may represent local reaction to a systemic disease, or a localized antigen-antibody reaction, and are classified as idiopathic. (Guray *and Sahin 2006)*

Acute Mastitis (lactational mastitis)

It is the commonest true inflammatory disease of the breast, cracked nipple allows bacteria to gain entry and stasis of milk provides the ideal condition for bacterial proliferation *(Rosen et al., 2001).*

Granulomatous Mastitis

Resulting from an infectious etiology, foreign material, or systemic autoimmune diseases such as sarcoidosis and Wegener's granulomatosis can involve the breast. Identification of the etiology requires microbiologic and immunologic testing in addition to histopathologic evaluation. (Guray *and Sahin, 2006)*

Foreign Body Reactions

Most foreign body granulomata of the breast are due to the introduction of prosthetic materials for cosmetic purposes. Silicone liquid is one of the most frequently used, producing large round empty-spaces surrounded by histocytes with vacuolated cytoplasm and multinucleated giant cells. The ensuing fibrosis may produce hard breast lumps and cause considerable distortion of the breast. *(Bartow, 2001)*

Recurring Subareolar Abscess

Is a rare bacterial infection of the breast that is characterized by a triad of draining cutaneous fistula from the subareolar tissue; a chronic thick, pasty discharge from the nipple; and a history of multiple, recurrent mammary abscesses. (Guray *and Sahin, 2006)*

Mammary Duct Ectasia

This disorder tends to occur in the fifth or sixth decade of life, Usually in multiparous women, and unlike periductal mastitis, is not associated with cigarette smoking. Patients present with a poorly defined palpable periareolar mass, sometimes with skin retraction, often accompanied by thick, white nipple secretions, pain and erythema are uncommon *(Lester et al., 2005).*

Duct ectasia refers to the presence of dilated large and intermediate ducts of the breast containing pasty, inspissated material with accompanying peri-ductal inflammation and fibrosis. This lesion is of clinical significance because the formation of an irregular mass can be mistaken for a carcinoma by palpation and by mammographic examination *(Lester et al., 2005).*

Fat Necrosis

Grossly, the lesion feels hard, irregular and may resemble carcinoma in the late sclerotic phases of the process. *(Bartow, 2001)*

Microscopically: it is characterized by anuclear fat cells often surrounded by histiocytic giant cells and foamy phagocytichistiocytes. *(Guray and Sahin,2006)*

Fibrocystic changes

Benign breast disorders and pathology under the designation of "fibrocystic disease". This term, when applied to a biopsy or a palpable breast mass, is nonspecific and often includes normal physiologic and morphologic changes in the breast along with specific benign disease process. *(Memon et al,2007)*

Fibrocystic disease (Mammary dysplasia)

This is a benign alteration of the breast, consisting of cystic dilatation of intralobular glands (terminal duct-lobular unit) with or without stromal fibrosis. Fibrocystic changes include apocrine metaplasia, mild epithelial hyperplasia, and mild degrees of adenosis. The etiology is hormonal imbalances with a predominance or relative excess of estrogens. . *(Moinfar, 2007).*

Intraductal Papilloma and Papillomatosis

Papillomas are composed of multiple branching fibrovascular cores, each having a connective tissue axis lined by luminal and myoepithelial cells. Growth occurs within a dilated duct. Epithelial hyperplasia and apocrine metaplasia are frequently present. Large duct papillomas are usually solitary and situated in the lactiferous sinuses of the nipple. Small duct papillomas are commonly multiple and located deeper within the ductal system. Small duct papillomas show increase the risk of subsequent carcinoma. *(Lester et al., 2005)*

Proliferative stromal lesions

Diabetic Fibrous Mastopathy

Diabetic fibrous mastopathy is an uncommon form of lymphocytic mastitis and stromal fibrosis. It occurs both in premenopausal women and (rarely) in men with long-standing type 1 insulin-dependent diabetes mellitus, who have severe diabetic microvascular complications.The mammographic and sonographic findings of these lesions are also highly suspicious for breast cancer, so a biopsy is

always essential for definitive diagnosis***(Guray and Sahin,2006)***

Pseudoangiomatous Stromal Hyperplasia of the Breast: Well-demarcated mass with a smooth external surface. The cut surface consists of homogeneous white and rubbery tissue***.(Guray and Sahin,2006)***

Neoplasms

Fibroadenoma

Grossly, the lesion is a well-circumscribed, firm mass, <3 cm in diameter, the cut surface of which appears lobulated and bulging .If the tumor assumes massive proportions (>10 cm), more commonly observed in female adolescents, it is called giant fibroadenoma. (Guray *and Sahin ,2006)*

Lipomas

A benign, well-circumscribed tumor with a delicate capsule consisting of fat cells without atypia. *Grossly:* solitary soft and well-delineated tumor with lobulated yellow cut surface. *(Moinfar., 2007).*

Adenoma

An adenoma is pure epithelial neoplasm of the breast. This lesion is divided into tubular, lactating, apocrine, ductal, and so-called pleomorphic (i.e., benign mixed tumor) adenoma. Both lactating and tubular adenomas occur during the reproductive ages. (Guray *and Sahin ,2006)*

Nipple Adenoma

Nipple adenoma, also known as florid papillomatosis of the nipple ducts or erosive adenomatosis, is a benign tumor of the ductal epithelium that often clinically mimics Paget's disease and pathologically may be misinterpreted as an adenocarcinoma. (Guray and Sahin ,2006)

Hamartoma

A well-circumscribed, usually encapsulated nodule consisting of all breast tissue components, often with an abnormal proportion (malformation). *Grossly*, a well-demarcated, sometimes lobulated mass, often rubbery greyish-white to yellow cut surface, resembling fibroadenoma or lipoma. *(Moinfar., 2007).*

B-Malignant Breast Lesions

a-Non- Invasive Carcinoma

Intraductal carcinoma in situ

Ductal carcinoma in situ (DCIS) is defined as proliferation of epithelial cells within the parenchymal structures of the breast and is distinguished from invasive carcinoma of the breast by the absence of microscopic stromal invasion across the limiting basement membrane. *(Faverly et al,1994)*

Comedocarcinoma

Comedocarcinoma is characterized by solid sheets of pleomorphic cells with high-grade nuclei and central necrosis. The necrotic cell membranes commonly calcify and are detected on mammography as clusters or linear and branching micro-calcifications. periductal concentric fibrosis and chronic inflammation are common and extensive lesions are sometimes palpable as an area of vague nodularity *(Lester et al., 2005).*

Lobular carcinoma in situ (LCIS)

Grossly, the acini are distended and filled by neoplastic cell.

Microscopically, the majority of these cells are uniform and slightly larger than the normal cells. These cells are intermingled with larger cells with prominent nucleoli. The involved lobular acini often surround normal ducts. ***(Bartow, 2001)***

b-Invasive Carcinoma

Invasive duct carcinoma (NOS)

there is a marked variation in size, from smaller than 1 cm to larger than 10 cm. The tumors can have an irregular, stellate outline or a nodular configuration with pushing margins. There is usually a greyish-white cut surface with hard consistency. Carcinomas frequently feel gritty when cut with a knife, yellow to white streaks can be present. The fatty tissue close to the tumor often reveals an intense yellow color that differs from the color of fatty tissue away from the carcinoma (Fig. 6b) *(Moinfar., 200.*

Invasive lobular carcinoma (ILC)

Typically, invasive lobular carcinoma forms a firm to hard tumor with irregular borders. Another gross manifestation of invasive lobular carcinoma (ILC) is the formation of numerous small hard nodules mimicking sclerosing adenosis. ***(Moinfar., 2007).***

Medullary carcinoma

Grossly, the typical medullary carcinoma is well circumscribed, has a soft and uniform consistency, and measures between 1 and 4 cm in diameter. ***(Bartow, 2001)***

Mucinous carcinoma

Mucinous carcinoma consists of well differentiated nests of tumor cells freely floating within pools of mucin . Mucinous carcinoma is often quite hypocellular, and the bulk of the lesion may be mucin with relatively few clusters of tumor cells ***(Kopans, 2007).***

Paget's disease

Clinically, it presents with roughing, reddening and erosion of the nipple. The clinical features may be indistinguishable from eczema or other chronic forms of dermatitis. Any nipple lesion with such features, particularly if it fails to heal rapidly, should be regarded as suspicious of Paget's disease and be biopsied. ***(Bartow, 2001)***

Tubular carcinoma
Tubular carcinoma consists of well-differentiated tumor cells forming well defined simple tubules or glands, usually embedded in a fibrotic or fibroelastotic stroma.

Adenoid cystic carcinoma
It usually represents as a mass lesion. It is a rare form of breast tumors. They are recognized to have an extremely good long-term prognosis. Metastatic spread, although rare, does occur. ***(Cornford et al, 1995)***

Invasive papillary carcinoma
Invasive carcinomas with a papillary architecture are rare, and represent 1% or fewer of all invasive cancers.

Special types of breast carcinoma
Inflammatory carcinoma
Is a clinical description of invasive carcinoma with extensive involvement of dermal lymphatic spaces. The obstruction of the dermal lymphatics by tumor causes hydrostatic obstruction in the skin, resulting in marked tissue edema, engorgement, induration, and erythema. Skin sloughing, erosion, or ulceration can occur.

Minimal occult and early breast carcinoma
The term "minimal breast cancer" refers to heterogeneous group of non-invasive carcinoma of either ductal or lobular type, as well as invasive carcinoma having a size less than 1 cm in diameter. This includes all carcinomas confined to the breast without axillary node metastases. Minimal breast carcinoma should be distinguished from occult breast cancer; the latter refers to a non-palpable, asymptomatic, and to some cases not even mammographically demonstrable. ***(Blamey, 1998)***

Microinvasive carcinoma
It is defined as a tumor in which the dominant lesion is non invasive but shows one or more clearly separate small microscopic foci of infiltration into the breast stroma. ***(Moinfar., 2007).***

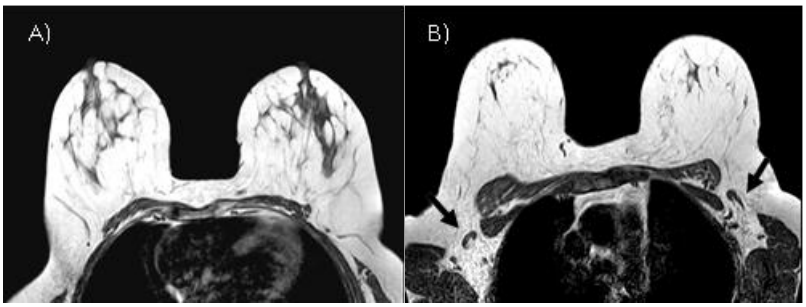
Infiltrating carcinoma presenting as axillary mass
Breast carcinoma may present as axillary mass in the absence of a clinically, detectable breast tumor. It is possible that some of these tumors actually arise from either the axillary tail of the breast, accessory breast tissue in the axilla, or heterotrophic breast tissue in an axillary lymph node. ***(Blamey, 1998)***

Diffusion Weighted Imaging on the DETECTION of Breast Lesions
In oncologic imaging, DW-MRI has been linked to tumor response. Parameters derived from DW-MRI are appealing as imaging is noninvasive, does not require any exogenous contrast agents, does not use ionizing radiation yet is quantitative and can be obtained relatively rapidly, and is easily incorporated into routine patient evaluations**.**

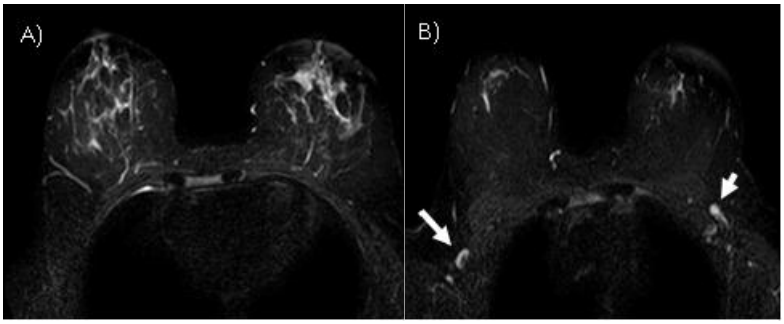
Superadded value of Diffusion in diagnosing breast lesions
The excellent sensitivity of breast MRI has proven particularly advantageous in the preoperative patient, its limited specificity continues to be a significant problem, particularly in patients referred for further clarification of an inconclusive finding obtained by conventional breast imaging.

Case presentation
Case No. (1)
Clinical background
Thirty-five years old patient complains of bilateral mastalgia. Fibroadenosis was suggested on clinical and sonomammographic examination, yet she needed further check up

Dynamic MR of the breast

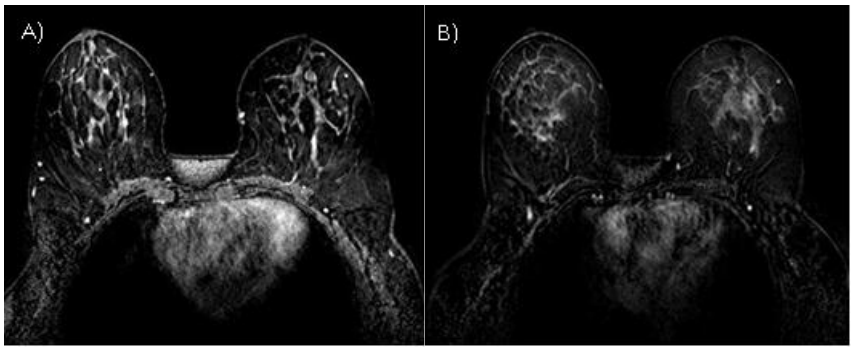


Axial T1 SE (TR/TE 500/5.3 msec., slice thickness: 4 mm). A) Both breasts show intermediate SI normal glandular tissue, bright SI fat & normal skin/nipple. B) Normal axillary nodes (arrows) that show thin intermediate SI cortex &bright central fatty hilum.

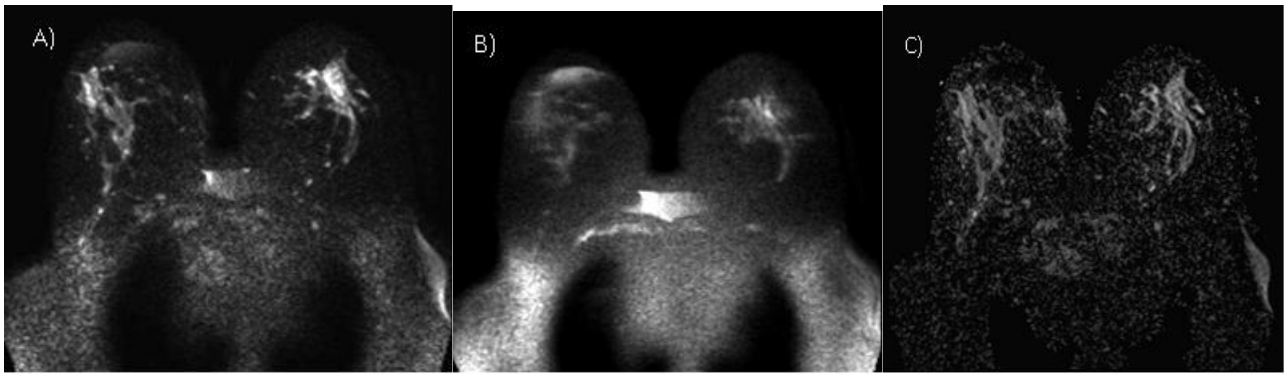


Axial T2 STIR (TR/TE 4000/1.2 msec., slice thickness: 4 mm). A) Both breasts show diffuse bright SI of the glandular tissue, in correlation with the clinical compliant of mastalgia, finding suggests adenosis. Note suppressed dark fatty tissue.

A) Axillary nodes (arrows) show bright SI cortex &suppressed dark fatty hilum.



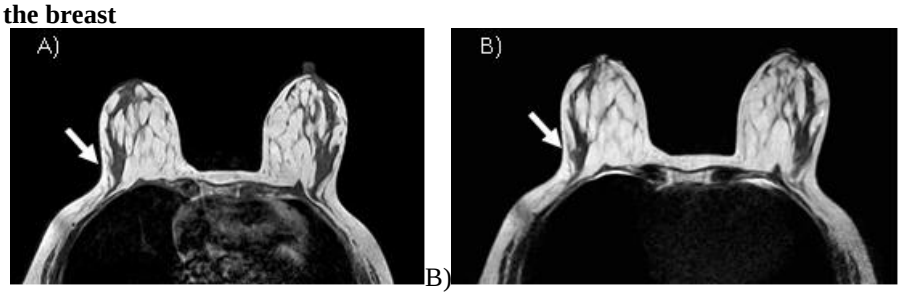
Axial dynamic post contrast THRIVE (T1W high resolution isotropic volume examination) (TR/TE 2.8/9 msec., slice thickness: 1.5 mm). A) Both breasts at 3 min. series of the dynamic sequence. B) Subtraction pre-from post contrast series at 3 min. Normal enhancement pattern of the glandular tissue.



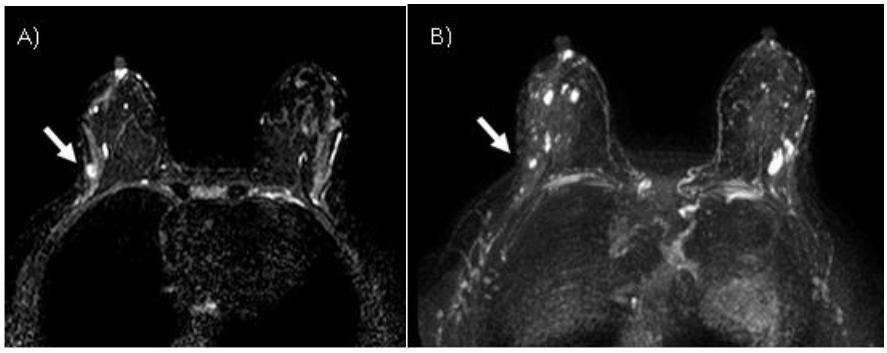
Axial DWI (EPI) and post processing ADC map. A) b0, B) b600. C) ADC map. Diffusion sequence showed diffuse slightly bright SI of the glandular tissue consistent of slight water restriction (i.e. congestion and consequently adenosis). ADC values using ROI at different locations revealed 1.39 and 1.5 x 10^{-3} mm^2 /s (acceptedconsidered normal ADC value of the glandular tissue).

Case No. (2)
Case presentation
Benign mass
Clinical background
Forty years old patient.
Previous sonomammography: Right breast upper outer focal solidbenign looking mass
Pathology: adenoma

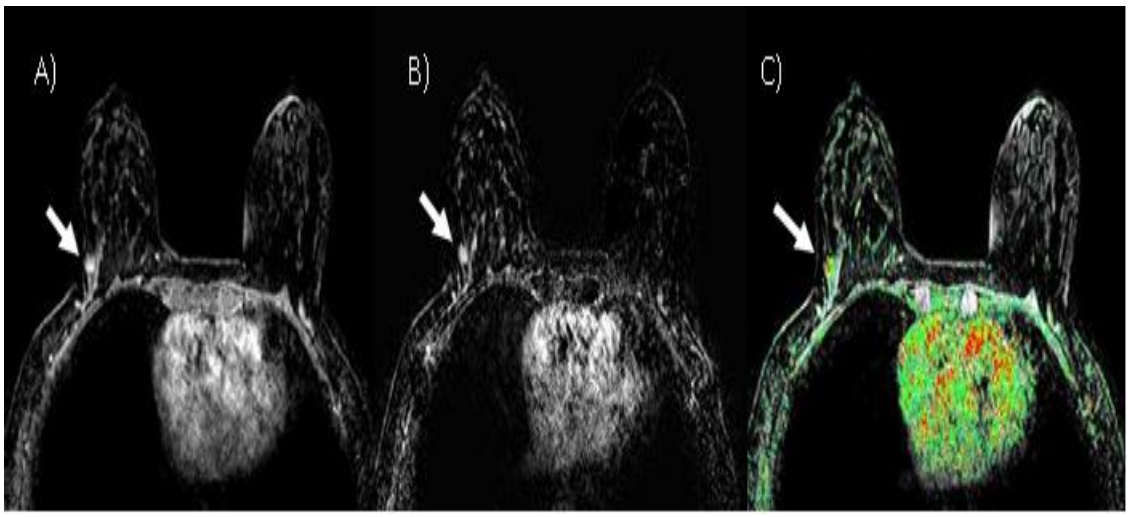
Dynamic MR of the breast



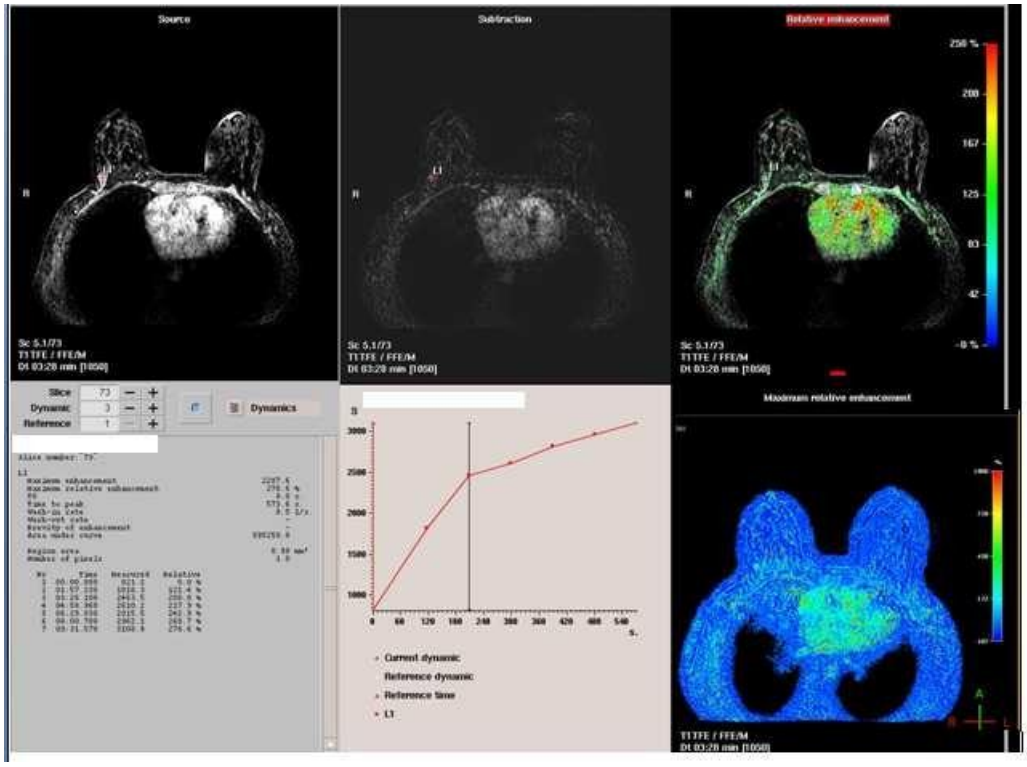
Axial A) T1WI SE and B) T2WI that show right breast upper outer tiny focal mass (arrow) of intermediate SI inconisopous from the related glandular tissue on T1WI and slightly bright on T2WI

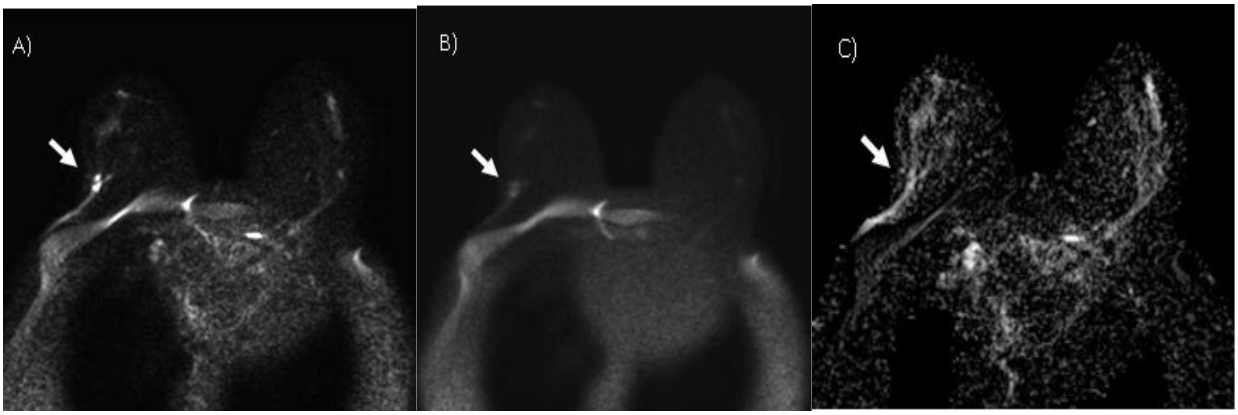


Axial A) T2 STIR and B) 3D reconstructed MIP of the same sequence. Right breast upper outer tiny focal well-defind mass (arrow) of bright SI, the other bright SI masses seen in both breasts at the MIP reconstructed image representassociate simple cysts



Axial A) dynamic THRIVE sequence and B) subtraction image at 5.4 minutes post contrast IV injection. Right breast upper outer homogenously enhancing focal tiny mass (arrow). C) The same post contrast image with color overlay Time/signal intensity analysis of the region of interest (ROI). Right breast upper outer quadrant mass shows progressively rising benign curve pattern (Type I) with early peak of contrast uptake and corresponding SI % of 278 %.



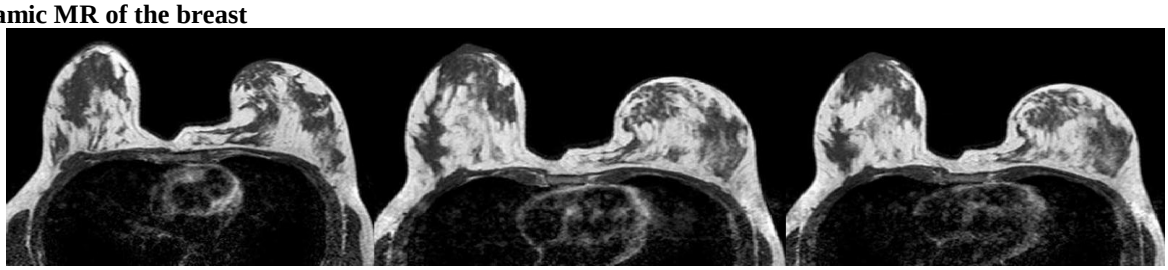


Diffusion sequence and post processing ADC map that shows right breast upper outer tiny mass of benign criteria. A) b0, B) b600. C) ADC map. ADC value forthe region of interest was 1.2 x 10^{-3} mm^2 /s.

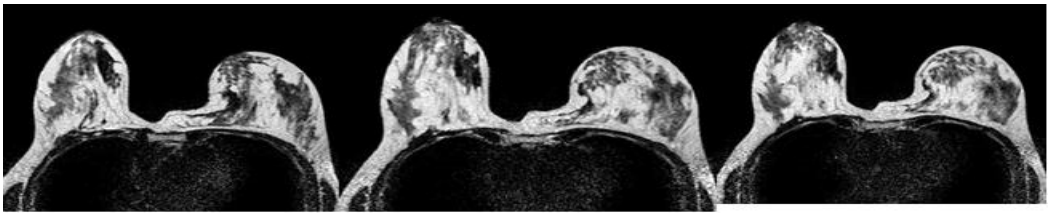
Case No. (3)
Case presentation

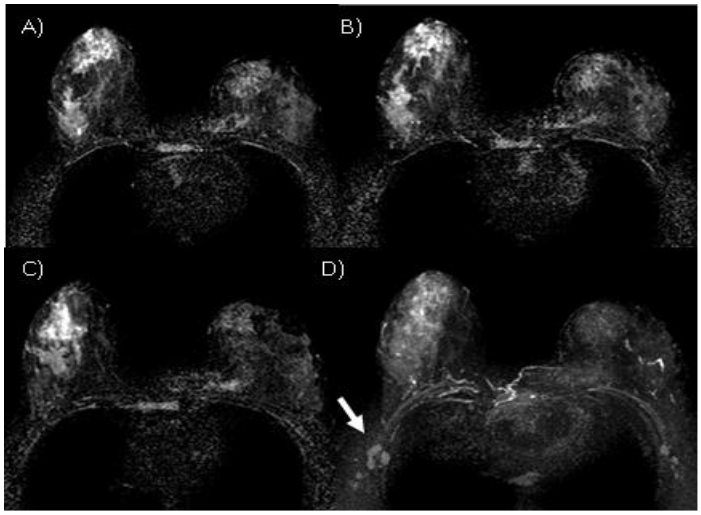
Malignant mass
Clinical background
Forty- eight years old patient.
Previous sonomammography: Right breast upper outer and outer central multicentric suspicious probably malignant connective tissue infiltration ***Pathology:*** Multicentric invasive ductal carcinoma grade 2.

Dynamic MR of the breast

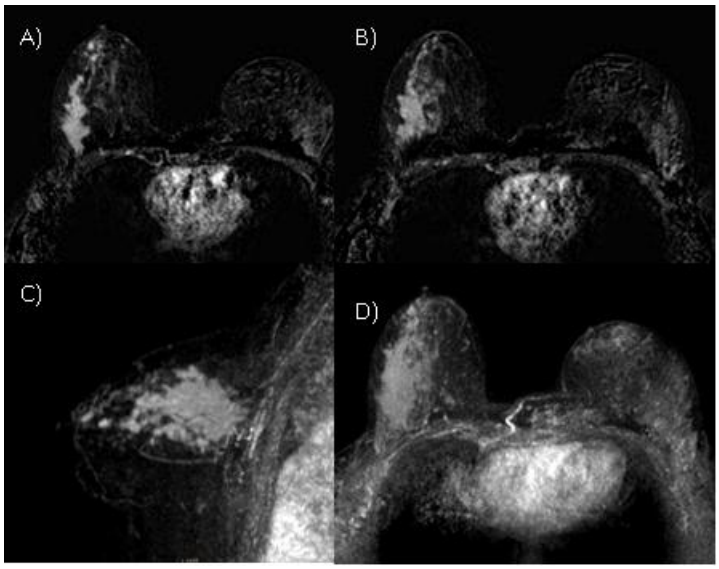


Axial T1 & T2WI. The above row is T1WI sequence and the below row isT2WI sequence, the right breast shows ill-defind soft tissue infiltrative lesion hat involves the entire upper outer quadrant that elicits the same SI of the glandular tissueon T1WI and intermediate-slightly bright SI on T2WI.

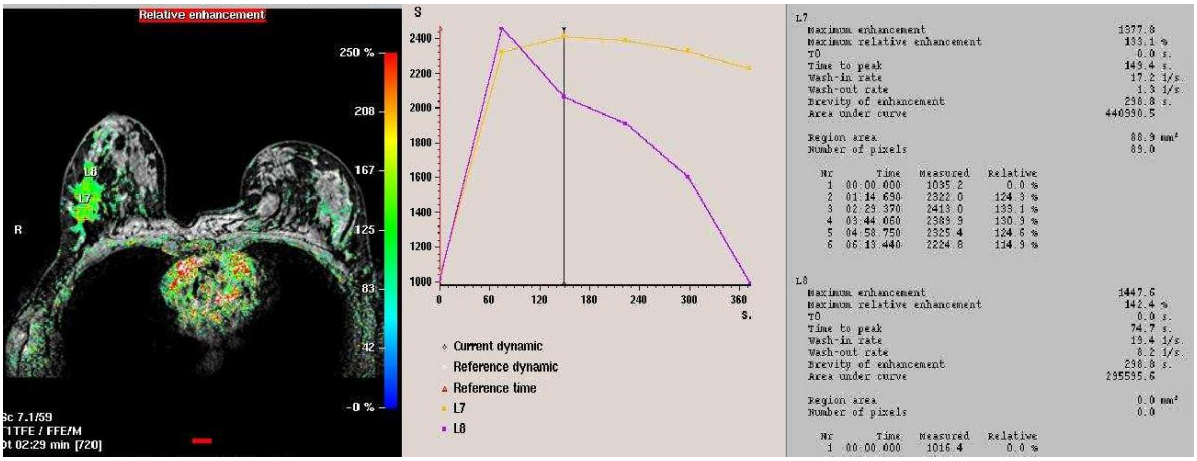




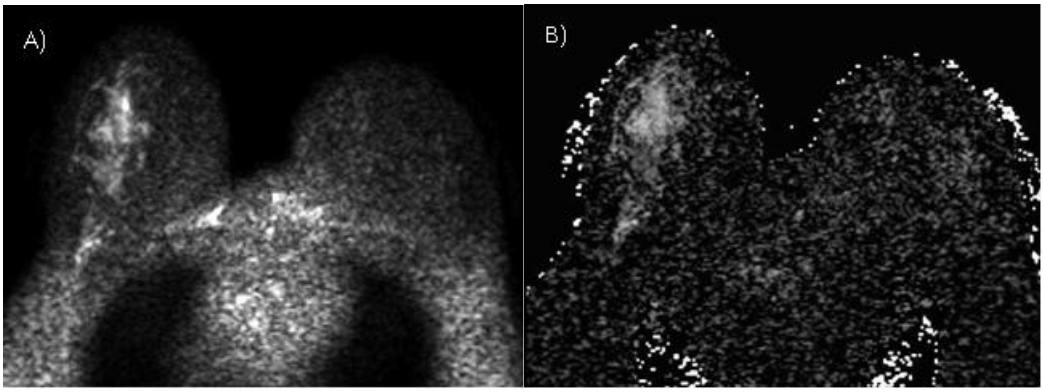
Axial T2 STIR and 3D reconstructed MIP. A),B) &C) The right breast lesion of question displayed intermediate –low SI, there is related tissue traction and bright SI edematous changes that extends towards the nipple/areola complex. D) The reconstructed MIP image shows the entire extend of the lesion as well as the subsequent tissue reaction and the ipsilateral enlarged axillary nodes (arrow).



A) &B) Axial subtraction sequence of dynamic pre- and post contrast 2 min. series of that right breast multicentric mass that show early inhomogeneous beaded enhancement. C) & D) Sagittal and axial 3D MIP reconstructed images.



Time/signal intensity analysis of the region of interest (ROI). Right breast lesion shows early peak of contrast uptake at 2.3 min. with corresponding SI % of 133-142 % followed by wash out (type III- malignant pattern) and plateau (type II- suspicious pattern) curve.



Diffusion sequence and post processing ADC map that shows right breast upper outer and central extensive tissue infiltration and recognizable water restriction.

A) b 600 & B)ADC map. ADC value of the region of interest revealed 0.8 x 10^{-3} mm^2 /s

SUMMARY AND CONCLUSION

mammography and ultrasound remain the method of choice for routine screening programs and is the 1st imaging aid, but conventional assessment have well-known limitations, such as inaccurate differentiation between benign and malignant lesions and estimation of the size of malignant tumors.

The sensitivity of breast MRI for the detection of cancer is the greatest of all imaging techniques and when the findings of conventional imaging are inconclusive (i.e. BI-RADS 0), MRI can be used as a problem-solving modality, it is also better at identifying the true extent of cancer when multifocal disease or ductal carcinoma in situ is present.

Although contrast material–enhanced magnetic resonance (MR) imaging of the breast is exquisitely sensitive for detection of invasive breast cancer, its reported specificity is variable.

Diffusion-weighted imaging (DWI), if further clinical evaluation is needed, represents an easy non time consuming complementary quantitative breast imaging sequence. Based on diffusion properties; ADC mapping provides valuable information on benign and malignant lesions by characterizing tumor cellularity.

DWI has high specificity for breast malignant lesions and has the potential to analyze cancer extension. The ADC is a sensitive and specific parameter in differentiating benign and malignant breast lesions.

It must be understood that DWI can't stand alone as a diagnostic criterion to avoid non visualization of small breast lesions thus it must conjugate with contrast enhanced MRI, in this way it may improve the overall specificity of MRI for characterizing breast lesions

DWI has shown high sensitivity for breast cancer and is recommended as a part of routine preoperative examination and represents a promising tool for screening in the future especially for those who have sensitivity against contrast used in MRI examination.