CLINICAL EVALUATION OF DIFFUSION WEIGHTED IMAGING OF BREAST MASSES IN FEMALE PATIENTS FROM BIHAR REGION

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Abstract

Breast masses range from benign to malignant with varied etiologies. Fibroadenoma the Commonest benign and invasive ductal carcinomas are the commonest malignant lesions. Breast carcinoma is the most common and the second leading cause of deaths in women. It is present fully accepted that breast magnetic resonance is amongst the most sensitive diagnostic imaging techniques for breast lesions. DWI-MR (diffusion weighted magnetic resonance) provides new and different information about the biophysical properties of tissue. The consequent reduction of macroscopic motion effect makes possible the use of DWI in detection and characterization in breast MRI imaging. These facts and figures defines the need for early detection and treatment of breast for favourable prognosis. DWI has sufficient capacity to diagnose invasive, non-invasive breast lesions and has the ability to provide steady, high-resolution tissue images and there is a need to apply DWI to clinical practice while taking advantage of this high contrast resolution. Diffusion weighted Imaging is a potential resource as an adjuvant to breast MRI to differentiate benign from malignant lesions. Such sequence can be easily added to the standard breast magnetic resonance protocol.

The present study was planned in Department of Radio- Diagnosis, Katihar Medical College and Hospital, Katihar, Bihar, India. Total 20 cases of the breast lesions refereed to our hospital were evaluated in the present study. Those patients who had come for breast MRI examinations and were detected to have lesions greater than 1 cm in size were included in the study and DWI was performed after obtaining prior consent. Patients who were referred for mammography and sonomammography and who were detected to have solid lesions greater than 1 cm were also included in this study after obtaining prior consent; diffusion-weighted sequences were performed for these patients only to characterize the lesions detected on mammography and sonomammography.

The data generated from the present study concludes that DWI for breast lesions can differentiate benign from malignant lesions with a high sensitivity and specificity. The usefulness of this technique needs to be further evaluated with larger double-blind studies.

Keywords: Diffusion Weighted Imaging, DWI, Breast Masses, etc.

Introduction:

A breast mass, also known as a breast lump, is a localized swellings that feel different from the surrounding tissue. Breast pain, nipple discharge, or skin changes may be present. Concerning findings include masses that are hard, do not move easily, are of an irregular shape, or are firmly attached to surrounding tissue. Causes include fibrocystic change, fibroadenomas, breast infection, galactoceles, and breast cancer. Breast cancer makes up about 10% of breast masses. Diagnosis is typically by examination, medical imaging, and tissue biopsy. Tissue biopsy is often by fine needle aspiration biopsy. Repeated examination may be required. Treatment depends on the underlying cause. It may vary from simple pain

medication to surgical removal. Some causes may resolve without treatment. Breast masses are relatively common. It is the most common breast complaint with the women's concern generally being that of cancer.[1]

A breast cyst is a non-cancerous, fluid-filled sac in the breast. They generally feel smooth or rubbery under the skin and can be quite painful or cause no pain at all. Cysts are caused by the hormones that control the menstrual cycle and are rare in women older than 50. A sebaceous cyst is a non-cancerous, closed sac or cyst below the skin that is caused by plugged ducts at the site of a hair follicle. Hormone stimulation or injury may cause them to enlarge but if no symptoms are present, medical treatment is not required.[8]

Breast abscesses are non-cancerous pockets of infection within the breast. They can be quite painful and cause the skin over the breast to turn red or feel hot or solid. Abscesses of the breast are most common in women who are breast-feeding. Adenomas are non-cancerous abnormal growths of the glandular tissue in the breast. The most common form of these growths, fibroadenomas, occur most frequently in women between the ages of 15 and 30 and in women of African descent. They usually feel round and firm and have smooth borders. Adenomas are not related to breast cancer.[2]

Intraductal papillomas are wart-like growths in the ducts of the breast. These lumps are usually felt just under the nipple and can cause a bloody discharge from the nipple. Women close to menopause may have only one growth, while younger women are more likely to have multiple growths in one or both breasts. Breast cancer usually feels like a hard or firm lump that is generally irregular in shape and may feel like it is attached to skin or tissue deep inside the breast. Breast cancer is rarely painful and can occur anywhere in the breast or nipple.[2]

Breast masses are broadly classified as benign or malignant. Common causes of benign breast lesions include fibrocystic disease, fibroadenoma (see the image below), intraductal papilloma, and abscess. Malignant breast disease encompasses many histologic types that include, but are not limited to, in situ ductal or lobular carcinoma, infiltrating ductal or lobular carcinoma, and inflammatory carcinoma. The main concern of many women presenting with a breast mass is the likelihood of cancer. Reassuringly, most breast masses are benign.

The mammary glands arise from a caudal section of the ectodermal tissue known as the “milk lines,” which extend along the anterior surface of the developing fetus from the axilla to the groin. During puberty, pituitary and ovarian hormonal influences stimulate female breast enlargement, primarily owing to accumulation of adipocytes. Each breast contains approximately 15-25 glandular units known as breast lobules, which are demarcated by Cooper ligaments. Each lobule is composed of a tubuloalveolar gland and adipose tissue. Each lobule drains into the lactiferous duct, which subsequently empties onto the surface of the nipple. Multiple lactiferous ducts converge to form one ampulla, which traverses the nipple to open at the apex. [3]

Below the nipple surface, lactiferous ducts form large dilations called lactiferous sinuses, which act as milk reservoirs during lactation. When the lactiferous duct lining undergoes epidermalization, keratin production may cause plugging of the duct, resulting in abscess formation. [4] This may explain the high recurrence rate (an estimated 39%-50%) of breast abscesses in patients treated with standard incision and drainage, as this technique does not address the basic mechanism by which breast abscesses are thought to occur.

Postpartum mastitis is a localized cellulitis caused by bacterial invasion through an irritated or fissured nipple. It typically occurs after the second postpartum week and may be precipitated by milk stasis. There is usually a history of a cracked nipple or skin abrasion or failure to clean nipples after breastfeeding. Sleeping position may also affect the progression of mastitis to breast abscess. *Staphylococcus aureus* is the most common organism responsible, but *Staphylococcus epidermidis* and streptococci are occasionally isolated. Drainage of milk from the affected segment should be encouraged and is best achieved by continued breastfeeding or use of a breast pump. [5]

Nonlactating infections may be divided into central (periareolar) and peripheral breast lesions. Periareolar infections consist of active inflammation around nondilated subareolar breast ducts—a condition termed periductal mastitis. Peripheral nonlactating breast abscesses are less common than periareolar abscesses and are often associated with an underlying condition such as diabetes, rheumatoid arthritis, steroid treatment, granulomatous lobular mastitis, trauma, and smoking. Primary skin infections of the breast (cellulitis or abscess) most commonly affect the skin of the lower half of the breast and often recur in women who are overweight, have large breasts, or have poor personal hygiene. [6]

Breast masses can involve any of the tissues that make up the breast, including overlying skin, ducts, lobules, and connective tissues. Fibrocystic disease, the most common breast mass in women, is found in 60%-90% of breasts during routine autopsy. Fibroadenoma, the most common benign tumor, typically affects women aged 30 years or younger and accounts for 91% of all solid breast masses in females younger than 19 years. Infiltrating ductal carcinoma is the most common malignant tumor; however,

inflammatory carcinoma is the most aggressive and carries the worst prognosis. Mammary Paget disease, or adenocarcinoma of the nipple epidermis, is relatively rare but may be misdiagnosed as a benign dermatosis if care is not taken. [7]

Recurrent or chronic infections, pain, and scarring are causes of morbidity. Mastitis is usually seen in lactating women, but the presence in a nonlactating woman should spur evaluation for an inflammatory carcinoma, newly onset diabetes, infection with *Mycobacterium tuberculosis*, and other idiopathic causes. [8]

Abscess formation complicates postpartum mastitis in fewer than 10% of cases. Neonatal mastitis usually occurs in term or near-term infants, is twice as common in females, and progresses to development of a breast abscess in approximately 50% of cases. [9]

Diffusion-weighted magnetic resonance imaging (DWI or DW-MRI) is the use of specific MRI sequences as well as software that generates images from the resulting data that uses the diffusion of water molecules to generate contrast in MR images.[10] It allows the mapping of the diffusion process of molecules, mainly water, in biological tissues, in vivo and non-invasively. Molecular diffusion in tissues is not free, but reflects interactions with many obstacles, such as macromolecules, fibers, and membranes. Water molecule diffusion patterns can therefore reveal microscopic details about tissue architecture, either normal or in a diseased state. A special kind of DWI, diffusion tensor imaging (DTI), has been used extensively to map white matter tractography in the brain.

In diffusion weighted imaging (DWI), the intensity of each image element (voxel) reflects the best estimate of the rate of water diffusion at that location. Because the mobility of water is driven by thermal agitation and highly dependent on its cellular environment, the hypothesis behind DWI is that findings may indicate (early) pathologic change. For instance, DWI is more sensitive to early changes after a stroke than more traditional MRI measurements such as T1 or T2 relaxation rates. A variant of diffusion weighted imaging, diffusion spectrum imaging (DSI), was used in deriving the Connectome data sets; DSI is a variant of diffusion-weighted imaging that is sensitive to intra-voxel heterogeneities in diffusion directions caused by crossing fiber tracts and thus allows more accurate

mapping of axonal trajectories than other diffusion imaging approaches.[11]

Diffusion-weighted images are very useful to diagnose vascular strokes in the brain. It is also used more and more in the staging of non-small-cell lung cancer, where it is a serious candidate to replace positron emission tomography as the 'gold standard' for this type of disease. Diffusion tensor imaging is being developed for studying the diseases of the white matter of the brain as well as for studies of other body tissues (see below). DWI is most applicable when the tissue of interest is dominated by isotropic water movement e.g. grey matter in the cerebral cortex and major brain nuclei, or in the body—where the diffusion rate appears to be the same when measured along any axis. However, DWI also remains sensitive to T1 and T2 relaxation. To entangle diffusion and relaxation effects on image contrast, one may obtain quantitative images of the diffusion coefficient, or more exactly the apparent diffusion coefficient (ADC). The ADC concept was introduced to take into account the fact that the diffusion process is complex in biological tissues and reflects several different mechanisms.[12]

Diffusion tensor imaging (DTI) is important when a tissue—such as the neural axons of white matter in the brain or muscle fibers in the heart—has an internal fibrous structure analogous to the anisotropy of some crystals. Water will then diffuse more rapidly in the direction aligned with the internal structure, and more slowly as it moves perpendicular to the preferred direction. This also means that the measured rate of diffusion will differ depending on the direction from which an observer is looking.

Traditionally, in diffusion-weighted imaging (DWI), three gradient-directions are applied, sufficient to estimate the trace of the diffusion tensor or 'average diffusivity', a putative measure of edema. Clinically, trace-weighted images have proven to be very useful to diagnose vascular strokes in the brain, by early detection (within a couple of minutes) of the hypoxic edema. [13]

More extended DTI scans derive neural tract directional information from the data using 3D or multidimensional vector algorithms based on six or more gradient directions, sufficient to compute the diffusion tensor. The diffusion model is a rather simple model of the diffusion process, assuming homogeneity and linearity of the diffusion within each image voxel.[13] From the diffusion tensor,

diffusion anisotropy measures such as the fractional anisotropy (FA), can be computed. Moreover, the principal direction of the diffusion tensor can be used to infer the white-matter connectivity of the brain (i.e. tractography; trying to see which part of the brain is connected to which other part).

Recently, more advanced models of the diffusion process have been proposed that aim to overcome the weaknesses of the diffusion tensor model. Amongst others, these include q-space imaging [8] and generalized diffusion tensor imaging.

Breast masses range from benign to malignant with varied etiologies. Fibroadenoma the Commonest benign and invasive ductal carcinomas are the commonest malignant lesions. [14] Breast carcinoma is the most common and the second leading cause of deaths in women. [15] It is present fully accepted that breast magnetic resonance is amongst the most sensitive diagnostic imaging techniques for breast lesions. [16] DWI-MR (diffusion weighted magnetic resonance) provides new and different information about the biophysical properties of tissue. The consequent reduction of macroscopic motion effect makes possible the use of DWI in detection and characterization in breast MRI imaging. [17] These facts and figures defines the need for early detection and treatment of breast for favourable prognosis. DWI has sufficient capacity to diagnose invasive, non-invasive breast lesions and has the ability to provide steady, high-resolution tissue images and there is a need to apply DWI to clinical practice while taking advantage of this high contrast resolution. Diffusion weighted Imaging is a potential resource as an adjuvant to breast MRI to differentiate benign from malignant lesions. Such sequence can be easily added to the standard breast magnetic resonance protocol.

Methodology:

The present study was planned in Department of Radio- Diagnosis, Katihar Medical College and Hospital, Katihar, Bihar, India. Total 20 cases of the breast lesions refereed to our hospital were evaluated in the present study. Those patients who had come for breast MRI examinations and were detected to have lesions greater than 1 cm in size were included in the study and DWI was performed after obtaining prior consent. Patients who were referred for mammography and sonomammography and who were detected to have solid lesions greater than 1 cm were also included in this study after obtaining prior consent; diffusion-weighted

sequences were performed for these patients only to characterize the lesions detected on mammography and sonomammography.

In all patients, MRI was performed bilaterally. MRI examinations were performed using a 1.5-T MRI scanner (Magnetom Espree, Siemens Healthcare). Patients were examined in the prone position using a dedicated 4-channel phased array bilateral breast coil. Before administration of contrast media, axial bilateral fat-suppressed T2- weighted fast spin-echo, axial STIR, axial T1-weighted fast spin-echo and DWI series were acquired. DW image was performed in axial slice orientation using echo planar imaging pulse sequences incorporating with diffusion gradients.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Women of the age group 15 to 75 years and Breast lesions larger than 1cm detected by ultrasound/ mammogram.

Exclusion Criteria: Previous history of breast surgery within preceding 18 months Chemotherapy within preceding 18 months; Radiotherapy within preceding 18 months Lesions; smaller than 1 cm.

Results & Discussion:

Currently one of the most important indications for MRI is the differential diagnosis between cancer recurrence and surgical scar. In fact, breast MRI has become a common practice in the evaluation for recurrence of breast cancer. Both surgery and radiation can cause scarring with architectural distortion of the breast, which makes assessment of local recurrence difficult by means of clinical examination, mammography, and ultrasound. Post-treatment changes can mimic malignancy or obscure locally recurrent breast cancer. For these reasons, breast MRI is a useful tool in the evaluation of such patients. [18] Diffusion-weighted imaging (DWI) is an unenhanced MRI sequence that measures the mobility of water molecules in vivo and provides different and potentially complementary information to (Dynamic Contrast Enhancement) DCE-MRI. DWI is sensitive to biophysical characteristics of tissues, such as cell density, membrane integrity, and microstructure. Promising findings from preliminary

DWI studies of the breast have shown significantly lower apparent diffusion coefficient (ADC) measures for breast carcinomas than for benign breast lesions or normal tissue. [19] The lower ADC in malignancies is primarily attributed to higher cell density causing increased restriction of the extracellular matrix and increased fraction of signal coming from intracellular water. [20] A recent study reported high accuracy for characterizing enhancing breast masses through a multivariate combination of DWI and DCE-MRI features. [21]

Breast MRI is the widely accepted diagnostic approach for evaluating the breast. To improve the sensitivity of detecting breast cancer, several diverse techniques are used for breast MRI (21). In particular, dynamic-enhanced MRI provides for evaluating multiple foci of carcinoma in the breast and it displays extremely high sensitivity for identifying breast cancer. However, dynamic-enhanced breast MRI has some disadvantages such as being time-consuming and costly, the possible side effects of the contrast media and the relative low specificity compared to mammography and ultrasonography. [22]

Table 1: Age and Type of Lesions

Age Group	Benign	Malignant
20 – 30 years	2	1
31 – 40 years	3	2
41 – 50 years	4	2
51 – 60 years	2	1
60 years and above	0	3
Total	11	9

Table 2: Spectrum of Lesions

Lesion histopathology	Number of Cases
Duct ectasia	1
Fibrocystic disease	4
Fibroadenoma	1
Galactocele	0
Granulomatous mastitis	0
Infiltrating duct ca	7
Lipoma	1
Breast abscesses	1
Paget's disease of nipple	1
Phyllodes tumour	1
Scar	2
Seroma	1
Total	20

Table 3: Frequency of signal of lesions on T1WI

	Benign	Malignant
Hyperintense	1	1
Hypointense	10	7
Isointense	0	1
Total	11	9

Table 4: Frequency of signal of lesions on T2WI

	Benign	Malignant
Hyperintense	9	2
Hypointense	1	1
Intermediate	1	6
Total	11	9

Table 5: Correlation between MRI diagnosis and gold standard (HPR)

HPR Diagnosis	Benign	Malignant
<i>MRI Diagnosis</i>		
<i>Benign</i>	10	0
<i>Malignant</i>	1	7
Total	11	9

Table 6: Mean ADC value

	No. of Cases	Mean ADC value ($\times 10^{-3} \text{ mm}^2/\text{s}$)
<i>Benign</i>	11	1.21
<i>Malignant</i>	9	1.95

DWI is based on the principle of Fick's Law of concentration gradients and the Brownian movement of molecules. Malignant lesions, in general, have more tightly packed cells with a more compact architecture and, consequently, have lower ADC values as compared with benign lesions. There is inhibition of effective movement of water molecules and restricted diffusion in dense malignant lesions. The higher ADC values of cystic or necrotic areas reflect a lack of significant restriction of diffusion of water. [5] False-negative values can be obtained in cystic/necrotic malignancies. [23]

In the study conducted by Zhang et al. on 57 breast lesions, the threshold ADC value at b-1000 was $1.20 \pm 0.25 \times 10^{-3} \text{ mm}^2/\text{s}$. [6] They found that ADC values of malignant lesions were statistically much lower than benign lesions and peritumoral tissues. [24] The usefulness of contrast MRI in detecting breast malignancy was studied by Drew et al. in 334 women. [25] The sensitivity and specificity of dynamic contrast MRI in their study were 100% and 86% respectively for detecting malignant lesions. [7] In a study performed by Yabuuchi et al. to assess the utility of a combination of dynamic contrast MRI and DWI in lesion characterization, the sensitivity was found to be 92% and the specificity was found to be

86% for differentiating benign from malignant lesions. [26]

A study done by Yoshifumi Kuroki and Katsuhiro on 29 women with suspicious breast abnormalities showed that diffusion tensor imaging (DTI) may provide useful information to better characterize breast abnormalities on MRI. Malignant breast tumors demonstrated altered diffusion characteristics with significant differences in FA (fractional anisotropy) and ADC (apparent diffusion coefficient) compared to normal tissue and benign lesions, while benign lesions were not significantly different from normal tissue. [27]

In another study done by Mijung Park and Eun Suk Cha on forty one patients showed that DWI has a high sensitivity for detecting breast tumors and specificity for detecting malignant breast tumors. DWI was an effective imaging technique for detecting breast lesions, as compared using the T1 and T2 weighted images. [27]

In the study done by Lalita Pale and Balaji Reddy on 200 patients with solid breast lesions also the result was similar and showed that DWI is a useful technique for characterizing breast tumors, especially for lesions that cannot be adequately characterize by ultrasonography and routine magnetic resonance imaging. [28]

Conclusion:

The data generated from the present study concludes that DWI for breast lesions can differentiate benign from malignant lesions with a high sensitivity and specificity. The usefulness of this technique needs to be further evaluated with larger double-blind studies.

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