ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-7 | JULY-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

Dynamic Contrast enhanced MR Imaging of breast lumps: Correlating morphology & kinetic curves with histopathology.

Radiology

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ABSTRACT

Background: The diagnostic study was undertaken to evaluate the role of dynamic contrast enhanced MRI(DCMR) in the evaluation of breast lumps based on the morphological and kinetic characteristics.
Material and Methods: A study was done taking 70 patients of breast lump, who were found to have a BIRADS III or higher lesion on X-ray mammography. A DCMR was performed on these patients and histopthological correlation was done.
Results: DCMR was 100 % sensitive with a specificity of 76.19% in the diagnosis of malignancy. The negative predictive value was 100% and the positive predictive value was 90.74%.
Conclusion: We recommend that DCMR of the breast, being an excellent complimentary examination in the evaluation breast lumps be carried out prior to biopsy in BIRADS 3, 4 and 5 cases. Both morphology and kinetics need to be carefully analysed and importance given to the most ominous characteristic.

KEYWORDS:

Breast lump, Dynamic Contrast Enhanced MRI, BIRADS

Introduction

Breast cancer is the most common cancer in women worldwide and second most common after cervical cancer in India. It contributed to almost 12 % of total number of cases of cancer and 25% of total female cancers detected worldwide in 2014[1]. The incidence of this disease has been consistently increasing especially in the younger age group and in developing countries[2]. The high prevalence, increasing incidence in the younger age group and possibility of cure, if detected early makes early and accurate diagnosis vital in the management of breast cancer.

Breast imaging is performed using mammography which may be conventional or digital, ultrasound with elastography and magnetic resonance imaging (MRI). Other techniques like automated whole breast ultrasound, digital breast tomosynthesis and dedicated breast computed tomography are making gradual inroads.

The goals of breast imaging are to image the whole breast, detect mass lesions and areas of architectural distortion and determine whether these changes are due to a benign or a malignant process. In addition imaging also helps in obtaining tissue samples from the abnormal area.

MRI is an important modality in the evaluation of breast with its high soft tissue resolution, multi-planar cross-sectional capability and lack of ionising radiation. Dynamic contrast enhanced MRI(DCMR) of the breast is frequently used as an adjunct to mammography and ultrasonography to improve lesion detection, characterise primary as well as recurrent breast cancers and for evaluating response to therapy. MRI offers information on lesion morphology as well as functional aspects like tissue perfusion and enhancement kinetics[3].

Our study evaluated the role of dynamic contrast enhanced MRI in the diagnosis of breast lumps on the basis of morphological and kinetic assessment. We assessed the sensitivity and specificity of dynamic contrast enhanced MRI in diagnosing breast malignancies and also determined the positive predictive value of enhancement kinetics in delineating breast carcinomas from benign lesions.

Materials and Methods

A diagnostic study was undertaken at a tertiary care centre over a period of two years. Seventy female patients diagnosed as breast lump on clinical examination and subsequently found to have breast imaging-reporting and data system (BIRADS) III or above on X-ray mammography were included in the study. Patients in whom contrast MRI was contraindicated were excluded. The study was approved by our institutional ethics committee. Informed consent was taken from the patient.

DCMR was done using 1.5 Tesla (Symphony, Siemens Medical Systems, Erlangen, Germany) MR system with dedicated twin breast phased array coils for optimal signal reception. Gadolinium chelate as a contrast agent was administered intravenously at 0.1mmol/kg at 2ml/sec with saline flush. Dynamic scanning was done for 6 minutes after injection of intravenous contrast. Images so obtained were post processed at the work station and the regions of interest (ROIs) were placed in the area of interest as well as the normal tissues of the breast to obtain the kinetic curves.

The morphological analysis included the number of lesions, the location, consistency, shape, margins, skin and nipple changes. The graphs for patterns of enhancement were generated using the available software provided by the vendor. On the basis of the initial enhancement phase (within two minutes) and the delayed enhancement (after 2 minutes), lesions were classified into three basic enhancement patterns as illustrated in fig. 1.

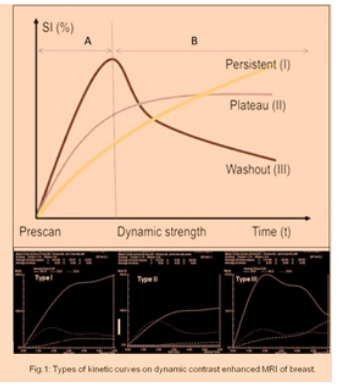

Fig.1: Types of kinetic curves on dynamic contrast enhanced MRI of breast.

A single BIRADS category was assigned based on the most suspicious finding (morphological or kinetic) on imaging.

The samples for histopathology were obtained by Tru-cut biopsy,

incision biopsy or excision biopsy. Where required imaging guided biopsy was performed using ultrasound guidance. In the patients who underwent surgery, histopathology of the surgical specimen was considered final. Fig. 2 illustrates the dynamic contrast enhanced MR evaluation of a breast mass.

Statistical analysis was done using appropriate tests for a diagnostic study.

Results

Age distribution of patients: The patients were divided into age groups 30-40years, 40-50years, 50-60 years and more than 60 years. In our study, the majority of the patient with breast cancer were in the 40-50 years age group.

Family History: A positive family history was recorded in 10 out of 70 cases i.e. 14.3% cases. Out of these nine cases were confirmed as malignancy on histopathology while one case was diagnosed as benign.

BIRADS category on X-ray mammography: As per our inclusion criteria, patients with BIRADS III or more were included in the study. Out of the 70 patients, 33(47.1%) were in BIRADS V category while there were 13 and 24 patients in BIRADS IV and III categories respectively. There was a significant association between mammographic grade and histopathological diagnosis, p value being <0.05.

Multiplicity of lumps: Clinically only 3 out of 70 patients had multiple lumps. MR however detected 19 patients with multicentricity or multifocality, 14 having a malignant lesion. There were also five patients in whom a lump was perceived clinically, but on MR assessment were found to have a diffuse lesion exhibiting non-mass like enhancement.

Shape of the lesion: We observed that 28 of the lesions were irregular in shape, 21 were lobulated, 12 were round and 4 cases were oval. An irregular shape had significant association with malignancy, while round and oval lesions were associated with benignity excepting one lesion in each category which turned out malignant.

Margins of the lesion: We could describe the margins in 65 lesions, the remaining being cases with diffuse non-mass enhancement. All cases with spiculated margins were found to be malignant on histopathology correlation indicating a 100% positive predictive value. Seventeen out of 25 cases (68%) with irregular margins and only one out of 11 cases (9%) with round margins were malignant. Five cases of diffuse non-mass like enhancement included two malignant and three benign lesions.

Consistency of the lesions: Most of the lesions i.e. 54 out of 65(83%) were solid and 11(17%) had either cystic or mixed solid-cystic composition. Five cases with non-mass like enhancement were not considered for evaluation of consistency.

Skin thickening and nipple retraction: On MRI assessment 19 cases had skin thickening as well as nipple retraction and the underlying lesion in all these cases proved to be malignant on histopathology.

Pattern of Enhancement: The various patterns of enhancement that were noted were heterogeneous (41 cases), homogeneous (12 cases), rim enhancement (9 cases), rim with nodular enhancement (3 cases) and non-mass like enhancement in 5 cases.

The association between pattern of enhancement on MR and histopathological diagnosis is given in Table 1. There was significant association between pattern of enhancement and histopathological diagnosis.

Pattern of enhancement on MRI	Histopathological diagnosis		Total	P-value
	Malignant	Benign		
Heterogeneous	38	3	41	< 0.001
Homogenous	4	8	12	
Rim & nodular enhancement	3	0	3	
Rim enhancement	2	7	9	
Non Mass	2	3	5	
Total	49	21	70	

Table 1: Association between pattern of enhancement on MRI & histopathological diagnosis

The types of kinetic curves obtained are given in Figure 1 above. A representative case with type III kinetic curve is shown in Figure 2.

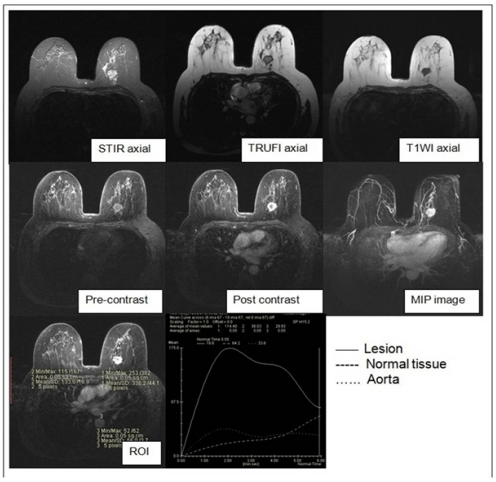

Fig 2: MRI Breast images showing morphology and type III kinetics of a mass lesion in the left breast. Histopathology revealed an invasive ductal carcinoma (Grade II)

There was statistically significant association between the kinetic curve and the histopathological diagnosis (Table 2).

Kinetic Curve on Contrast enhanced dynamic MRI	Histopathological diagnosis		Total	P-value
	Malignant	Benign		
I	1	12	13	< 0.001
II	6	7	13	
III	41	0	41	
Inconclusive	1	2	3	
Total	48	19	67	

TABLE 2: Association between kinetic curve and histopathological diagnosis

Final BIRADS categorization on DCMR: Our study included only those cases which were already categorized as BIRADS III and above on mammography. After complete morphological and functional assessment on dynamic contrast enhanced MRI, one case in X-ray mammography BIRADS III category was downgraded to BIRADS II and it turned out to be a benign pathology on histopathological evaluation following breast conservation surgery. Two cases in Xray mammography BIRADS IV category were also downgraded to BIRADS III on MR mammography and both were benign on histopathological analysis. Further MR mammography upgraded 10 cases with X-ray mammography BIRADS IV category to BIRADS V and all 43 cases given as BIRADS V on MR mammography were malignant on histopathological studies. All 15 cases given as BIRADS III proved to be benign and. Out of 11 BIRADS IV cases, 6 (54.55%) were malignant on histopathology. There was significant association between MR mammography, BIRADS grading and histopathological diagnosis (Table 3).

MRI BIRADS	MRI categorization of lesion	Histopathological diagnosis		Total
		Malignant	Benign	
IV and V	Malignant	49	5	54
II and III	Benign	0	16	16
Total		49	21	70

TABLE 3: Association between dynamic contrast enhanced MRI diagnosis and histopathological diagnosis

We analysed the performance of dynamic contrast enhanced MRI as compared to histopathology as gold standard. We considered BIRADS IV & V lesions as malignant and BIRADS II & III lesions as benign on MRI for statistical evaluation (Table 3). In our study MR mammography was 100 % sensitive though specificity was 76.19%. It reached a negative predictive value of 100 % however overall positive predictive value was 90.74% (Table 4).

Sensitivity	Specificity	PPV	NPV
100.00	76.19	90.74	100.00

TABLE 4: Performance characteristics of dynamic contrast enhanced MRI

An overview of histopathological diagnosis: Total 70 cases were studied, 49 cases were malignant and 21 benign. The histopathology of various lesions is shown in table 5.

Histopathological diagnosis	Number of cases	Percentage (%)
Infiltrating ductal carcinoma	41	58.6
Invasive lobular carcinoma	5	7.1
Medullary carcinoma	2	2.9
Ductal carcinoma in situ	1	1.4
Fibroadenoma	8	11.4
Fibrocystic disease	4	5.7
Hamartoma	1	1.4
Phylloides tumor	1	1.4
Others	7	10.0
Total	70	100.0

TABLE 5: Histopathological diagnosis of individual lesions

Discussion

'Detection' and 'diagnosis' are the two important cornerstones in the evaluation of breast lumps. The goal of breast imaging is to image the total mass of breast tissue, detect lesions and areas of architectural distortion, while discerning whether the observed changes are a benign or malignant process. X-ray mammography is the screening investigation of choice that has stood the test of time and usually is the first investigation in suspected breast lumps. There are two fundamental difficulties with mammography which make it less suitable for 'diagnosis'. Firstly, the radiographic density of glandular tissue is the same as the cancer being detected and secondly the visualisation of a 3-dimensional object as a single 2-dimensional image causes cancer to be hidden by the glandular tissue. Inclusion of supplemental examinations, such as ultrasound and MRI, are useful in further characterisation of lesion morphology which at times may be difficult by mammography alone.

MRI has a high soft tissue resolution and multi-planar cross-sectional imaging capability. The morphological characteristics of lesion, be it mammography or MRI, reflect the underlying process with the most aggressive forms having irregular shape and spiculated margins. However a malignant breast mass can vary in appearance on imaging. So, additional use of contrast-enhancement in MRI with dynamic studies adds functional information to the assessment i.e. internal enhancement pattern and kinetic information.

Morphological features of a lesion are important predictor of their pathology. Shape of masses can be divided into round, oval, lobulated and irregular with the probability of malignancy increasing as the lesion becomes more irregular in shape. Statistically, a lesion that is round or oval with sharply defined margins has a very high likelihood of being benign[5]. Some cancers can have a round or oval shape, the common type being medullary carcinoma, lymphoma, colloid cancer and papillary cancer[6]. In our study 96.4% lesion with irregular shape and 85.7% lesions with lobulated shape were proven to be malignant on histopathology. One round and one oval shaped mass were also found to be malignant, both being infiltrating ductal carcinoma (not otherwise specified). A careful analysis of the lesion margins with their functional assessment enabled us to suspect a malignant pathology in these cases.

We found lesion margin to be the most important morphological feature in differentiating benign from malignant lesion as is seen in number of previous studies[7,8,9]. All lesions with spiculated margins turned out to be malignant i.e. a 100% positive predictive value. These spiculations are produced due to the indrawing of the normal tissue towards the malignancy. Irregular margins were associated with malignancy in 68 % cases. Sometime even the classic lesion with a spiculated margin, which is almost invariably due to malignancy, is associated with a benign change such as sclerosing adenosis, a radial scar, an area of post-surgical change or fat necrosis[10]. However in our study we did not get such a case.

The consistency of the lesion is ascertained with T1 & T2 characteristics of the lesion. The lesions which are hyperintense on T2WI are usually benign except colloid carcinoma. Colloid malignancies, which contain abundant mucin, tend to be bright on T2WI fat saturated images[11]. Cystic lesions are intensely hyperintense on T2WI, hypointense on T1WI and usually show a rim enhancement. In our study there were four purely cystic lesions and all were well picked up on T2WI.

MRI of breast is highly sensitive in picking up multiplicity of disease which may get missed on X-ray mammography and physical examination In our study MRI picked up 19 cases with multiple lesions out of which 14 were malignant. Nine out of 14 malignant cases with multiple lesions were invasive ductal carcinoma. The selection for breast conservation therapy (BCT) depends on accurate assessment of the disease extent with multicentric, multifocal disease or bilateral disease being contraindication to BCT[12].

Even if the morphology of the lesion is completely defined it is sometimes not possible to differentiate benign findings from malignant due to an overlap of morphological characteristics. This is precisely why a functional assessment of lesion by using dynamic contrast enhanced MR is required. Enhancing lesions can be grouped into three categories: Masses, Non-mass-like enhancements and Focus (or foci). Masses are 3-dimensional structures with outward convex margins. Different patterns of enhancement are seen within masses. Homogenous enhancement is seen in benign lesions, however in our study it was seen in eight benign as well as four malignant cases. These four malignant cases with homogenous enhancement were histologically invasive lobular carcinoma and ductal carcinoma (not otherwise specified). Heterogeneous enhancement is more worrisome because it reflects a more irregular process typical of malignancy[13]. Heterogeneous enhancement was noted in 38 malignant masses and three benign masses in our study. In these benign masses the morphology of the mass and kinetic curves helped in indicating benignity of the lesion. The absence of enhancement on contrast administration is also an indicator of a benign lesion and has 88 % negative predictive value for cancer[14]. However we did not get any lesion showing complete absence of enhancement in our study. Two cases of fibroadenoma showed typical homogenous enhancement with dark non-enhancing internal septations as noted in number of other studies[15]. Enhancing septae are associated with malignant masses, however we did not find these septae in any of our cases. Except for purely cystic lesions, rim enhancement occurs due to central tumour necrosis and has a very high positive predictive value for malignancy at 79%-84%[16]. This finding on MRI needs to be looked at with a high index of suspicion. In our study, two out of nine cases with rim enhancement were malignant. Rest of the seven cases displaying rim enhancement were mostly benign cysts on histopathology. The rim in malignant cases was thick, irregular and had associated enhancing solid nodules. The other form of enhancement is non-mass like enhancement, which can be further characterised in various patterns like focal, ductal, linear, segmental, regional and diffuse non mass like enhancement. These patterns also have different form of internal enhancements like homogenous, heterogeneous, punctate and clumped internal enhancement[17]. In our study we observed five cases of non-mass like enhancement. Two cases of non-mass enhancement were malignant on histopathology. On imaging both had the segmental and the regional pattern of non-mass like enhancement with 'clumped up' internal enhancement. Segmental pattern of non-mass like enhancement has the highest PPV (PPV 100%) for carcinoma[18].

The breast mass enhancement was characterised quantitatively by assessing the enhancement kinetics curve. Based on the analysis of the initial slope of increasing enhancement from the baseline to the peak and the subsequent trend, three patterns were identified.

Type I is a pattern of progressive enhancement, with continuous increase in the signal intensity on each successive contrast-enhanced image. Type II kinetics is with a plateau pattern whereas type III curve indicates rapid wash in & wash out of contrast. As per a study done by Kuhl et al, the distribution of curve types for breast cancers was type I, 8.9%; type II, 33.6%; and type III, 57.4%[19]. In our study type I kinetics were associated with 12 benign lesions and 01 malignant lesions, type II with 6 benign masses and 07 malignant while type III kinetics was seen only in the 41 malignant cases(Fig 4). The positive predictive value of kinetic curve for malignancy in our study was 7.7 % for lesions with type I curve, 46.15% for type II curves and 100% for type

III curves. If type II and III curves (i.e. plateau and washout time courses) are used as criteria to diagnose breast cancer, a positive predictive value of 87% was observed (47 malignant lesions out of 54 type II & type III curves) in our study, where as Kuhl et al found it to be 77%.

We recommend that kinetics needs to be read in conjunction with the lesion morphology and the most suspicious characteristic should dictate the further course of action.

In addition to characterizing the mass, we found MRI provided excellent assessment of the surrounding structures such as adjacent parenchyma, skin, nipple, pectoralis muscle, chest wall and axilla.

In our study BIRADS II and III category were given to one and 15 patients respectively, all of which turned out to be benign. BIRADS IV category in 11 patients correlated to six malignancies and five benign cases suggestive of 54.55 % likelihood of malignancy in lesions labelled as BIRADS IV on MRI. All 43 cases in BIRADS V category were found to be malignant on histopathology.

The overall sensitivity and specificity of the dynamic contrast enhanced MRI in our study was 100 % and 76.19% respectively with a positive predictive value of 90.74% and negative predictive value of 100%.

Conclusion

The study attempted to evaluate the performance of contrast enhanced magnetic resonance imaging in suspicious breast lumps. We found that shape & margins of lesion in morphological assessment and pattern of enhancement with kinetic curve types in functional assessment had statistically significant association with histopathological diagnosis. Irregular and lobulated shapes indicated malignancy. Spiculated margins of a lesion had almost 100 % positive predictive value for malignancy. Type III kinetic curve was a depicter of malignancy with 100 % positive predictive value. Type I curve was seen mostly in benign cases. Type II curve was seen in 46.15 % benign cases and 53.85% malignancies. If type II and III kinetic curves were used as criteria to diagnose breast cancer, a positive predictive value of 87% was observed. DCMR was 100 % sensitive with a specificity was 76.19%. It reached a negative predictive value of 100 % however overall positive predictive value was 90.74%. We recommend that dynamic contrast enhanced MRI of the breast, being an excellent complimentary examination in the evaluation breast lumps be carried out prior to biopsy in BIRADS 3,4 and 5 cases.

Conflict of Interest: All authors have none to declare.

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