ROLE OF CONTRAST MR MAMMOGRAPHY IN THE INDETERMINATED BREAST DISEASES

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ABSTRACT

The purpose of this study is to evaluate the diagnostic capability of contrast MR mammography (MRM) in the problem of breast lesions that were indeterminated on mammography and ultrasonography.

The contrast MRM of twenty - two proven breast lesions was retrospectively reviewed. All lesions were indeterminated on mammography and sonography. There were eight cases received conserving breast treatment for carcinoma. The contrast MRM was performed by GE Signa 1.5 Tesla system. Only nine cases had post contrast dynamic study with signal time curve. All lesions were read and concensus by two radiologists using the same criteria based on MR morphologic features, patterns of enhancement and signal time curve. The qualitative and quantitative studies were integrated into the five points confidence scale (MRI score). The lesions were graded benign or malignant according to the MRI score (1,2 = benign and 3,4,5 = malignant). Furthermore, we analyzed the data of these lesions into two groups, group 1 without signal time curve and group 2 with signal time curve.

Twenty - two lesions were interpreted by using the MRI score, seven lesions were considered to be malignant and fifteen lesions were considered to be benign. The sensitivity, specificity, and accuracy in the diagnosis of breast disease were 75%, 92.8%, and 86.4% respectively. In comparison between the group 1 and group 2, the sensitivity, specificity, and accuracy in diagnosis were 60.0%, 80.0%, 70.0% in group 1 and 100%, 100%, 100% in group 2, respectively.

Contrast MRM is the effective imaging method for evaluation of the breast lesions that mammography and sonography were indeter-minated. Supplement dynamic study with signal time curve should improve the capability and provide superiority in establishing the correct diagnosis.

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INTRODUCTION

Since the sensitivity of mammographic detection of lesions is reduced in dense breasts, augmented breasts and post conserving breast therapy whereas MRI of the breasts is increasingly used in addition to conventional mammography and ultrasonography. It is used to help patients with inconclusive findings of conventional breast imaging and to diagnose primary and recurrent breast cancer.[1-9]

Although the sensitivity and specificity of MRI in the detection of breast cancer have been reported in various studies. The sensitivity and specificity depend not only on criteria of interpretation, MRI technique and patient selection but also on the experiences of the radiologist. MRI of the breasts has been used in King Chulalongkorn Memorial Hospital since 1994. At the early time of the study, we used the shoulder coil and body coil for breast imaging, by the end of 1997 the bilateral breast surface coils were available. The goal of our study is to evaluate the diagnostic capability of contrast MR mammography (MRM) in those patients with indeterminated lesions by mammography and ultrasonography.

MATERIALS AND METHODS

We retrospectively reviewed MRI records in our Hospital since December 1994 to August 1999. Twenty contrast enhanced MRI studies of the breasts with available medical records were included in the study. All cases had mammography and ultrasonography performed showing indeterminated lesions. Eight cases had a history of carcinoma of the breast received conserving breast treatment with problem of residual tumor or fibrosis. The patient's age varied between 26-72 years old (mean = 46.7 years). Nineteen cases were female and one case was male. One of the women had 3 MRI studies of the breasts, one for the left breast and two for the right breast at different times. The final diagnosis was established by means of fine needle aspiration cytology (FNAC), biopsy or follow up by physical examination and mammography.

MRI studies of the breasts were performed by GE Signa 1.5 tesla system using a variety of imaging parameters, all with gadolinium contrast enhancement. Imaging protocols consisted of axial and sagittal spin echo T1W, axial or sagittal fast spin echo T2W images with fat suppression technique or short T1 inversion recovery (STIR) images. Post contrast enhanced dynamic study was performed in only 9 cases at 0, 1, 2, 3, 5 and 7 minutes by using 3D gradient echo images (SPGR) as well as the imaging subtraction and signal-time curve. Ten cases had been imaged in supine position using shoulder coil, two cases in prone position using body coil and the remaining eight cases had been used bilateral breast surface coils.

All qualitative images and quantitative analyses were reviewed by two radiologists and consensus was obtained for the MRI features without knowing conventional mammographic, sonographic and pathological findings. The MRI features were evaluated using these following criteria.

1. Lesion configuration. It was classified as a mass or non-mass related to the enhanced pattern as segmental, linear, regional or patchy. Regional and patchy configurations were both suggestive of benign breast changes.

2. Shape and borders. An irregular or even a spiculated shape was suggestive of malignant lesion, where as a round or oval shape suggested a benign mass.

3. The lesions internal architecture. The homogeneity and low signal internal septations both were suggestive of benignity. If it showed heterogeneous or peripheral enhancement (rim enhancement), this was suggestive of malignancy.

4. The signal time curve pattern was classified according to their shape as type I which was steady enhancement; type II, plateau of signal intensity; or type III, washout of signal intensity as shown in figure 1. A type I was indicative of benign lesion, where as type III strongly suggestive of malignancy. A type II may be found both in benign and malignant lesions.

Finally, the quantitative and qualitative assessments were combined into an integrated evaluation of the individual lesion rated on five points confidence scale (MRI score).

1. Definitely benign when morphological features were rated benign with homogeneous enhancement or type I signal time curve or when a non-mass related patchy or regional enhancement was found.
2. Probably benign when morphological features were rated benign with type II signal time curve or single morphological feature was rated malignant with type 1 signal time curve.
3. Possible malignant when one or two morphological features were rated malignant with patchy enhancement or type II signal time curve.
4. Probably malignant when single morphological feature was rated malignant with heterogeneous or rim enhancement or type III signal time curve.
5. Definitely malignant when all morphological features were characteristic of malignant with rim enhancement or type III signal time curve.

The classification of the lesions to be benign (negative) or malignancy (positive) depended on the MRI score, as shown in table 1. For calculation of sensitivity and specificity outcomes, the MRI score of 3, 4 and 5 were considered positive for malignancy while the MRI score of 1 and 2 were negative or benign. According to twenty-two lesions, twelve lesions were evaluated using signal time curve and ten lesions without using signal time curve.

Table 1. MRI score and lesion classification.

MRI SCORE	LESION
1, 2	Benign
3, 4, 5	Malignant

RESULTS

Twenty-two lesions were identified on MRI studies. Seven lesions were considered malignancy and fifteen lesions were considered benign on the basis of MRI score. The MRI classification related with the final diagnosis was shown in table 2.

According to the seven lesions considered malignancy on MRM, three lesions showed rim enhancement (Fig. 1), four lesions showed heterogeneous enhancement (Fig. 2). Three of seven lesions had signal time curve which showed to be type 3 in two lesions and type 2 in one lesion (Fig. 3 A,B). Among these seven lesions, six lesions were histological proven to be invasive ductal carcinoma. There was one case that MRM showed spiculated irregular lesion in left breast with heterogeneous enhancement and was

misinterpreted without signal time curve as malignancy (MRI score 4), this case had involuted asymetrical breasts on mammography and increased radiotracer uptake at left subareolar region on Tc^{99m} sestamibi. Needle-guide biopsy was finally performed and cytology showed to be adenosis. No malignant lesion was found during the follow-up time of 59 months.

In fifteen lesions of twelve cases considered benign related to MRI score 1 and 2 with benign morphological features and type 1 signal time curve (Fig. 4 A,B). Microdochectomy was performed in two cases and histopathology turned out to be intraductal papilloma. Fine needle aspiration cytology (FNAC) was performed in three cases and no malignant cell was found. One patient had biopsy, proved to be adenocarcinoma metastasis in an axillary lymph node without detectable primary tumor elsewhere. MRM of this case showed no definite mass or abnormal enhancement in both breasts and was diagnosed as occult breast cancer with axillary node metastasis. She was treated with axillary node dissection and systemic chemotherapy. One case had biopsy done and histopathology proved to be intraductal papillary carcinoma with foci of invasive tubular carcinoma. In the remaining eight cases, there was no lesion shown up after a period of follow - up time from 8 to 48 months (mean = 18.5).

The calculations of positive predictive value (PPV), negative predictive value (NPV), sensitivity, specificity and accuracy for the diagnosis of the breast disease were divided into three categories as shown in table 3, 4 and 5 since there were two different groups in MRI interpretation, one group (12 lesions) with MR signal time curve and the other (10 lesions) without signal time curve.

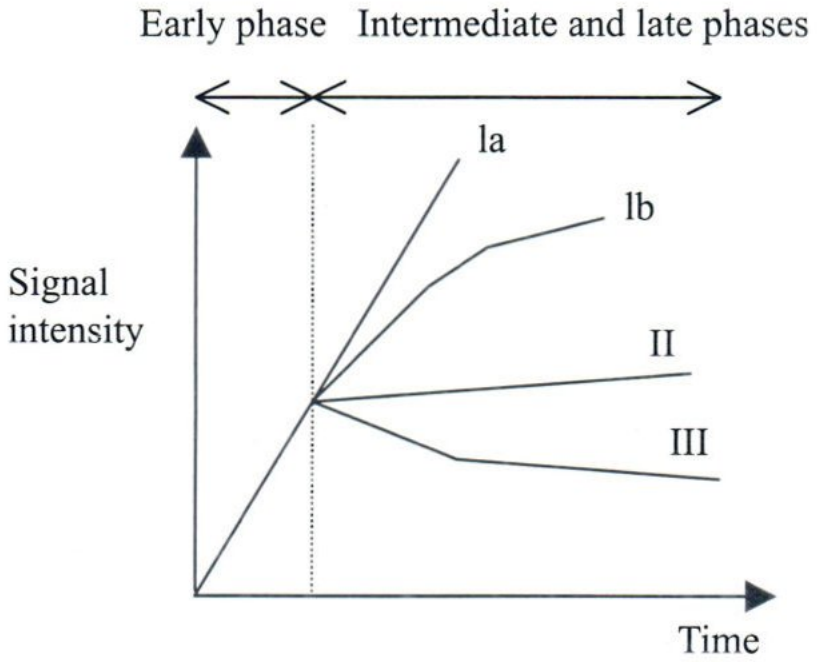


Fig. 1. Schematic drawing of the signal time curve types. Type I corresponds to a straight (Ia) or curved (Ib) line; enhancement continues over the entire dynamic study. Type II is a plateau curve with a sharp bend after the initial upstroke. Type III is a washout time course.[14]

Table 2. MRI score and breast lesion correlation.

No.	Age	coil	SI-T curve	MRI score	Conclusion	Remark
1.	34	shoulder	III	5	invasive ductal carcinoma	post conserving surgery
2.	62	"	I	1	benign (33 mo)	"
3.	50	breast	I	1	benign (16 mo)	"
4.	47	shoulder	-	2	benign (17 mo)	"
5.	52	"	-	5	invasive ductal carcinoma	"
6.	49	breast	I	1	benign (FNAC, 9 mo)	"
7.	43	"	III	5	invasive ductal carcinoma	"
8.	35	"	I	1	no malignant cell	post conserving surgery followed by mastectomy after 10 mo follow up.
9.	36	"	II	4	invasive ductal carcinoma	dense breasts
10.	55	shoulder	-	4	adenosis (needle-guide Bx, 59 mo)	asymmetrical breasts
11.	56	shoulder	-	5	invasive ductal carcinoma	male, mass in left breast
12.	54	body	-	1	adenocarcinoma of axillary node	left axillary mass
13.	26	breast	II	2	intraductal papilloma	right nipple discharge
14.	72	"	I	1	fibrofatty tissue (FNAC, 8 mo)	extensive fat necrosis
15.	45	body	-	2	intraductal papillary carcinoma with foci of invasive tubular carcinoma	left breast pain with bloody discharge
16.	45	shoulder	-	2	benign (48 mo)	palpable mass in Rt breast
17.	45	breast	II	1	benign (8 mo)	"
			II	2	benign (8 mo)	"
			II	2	benign (8 mo)	"
18.	54	shoulder	-	1	adenosis (FNAC, 57mo)	left breast pain, no palpable mass
19.	43	"	-	2	intraductal papilloma	right bloody discharge
20.	32	"	-	5	invasive ductal carcinoma	palpable mass

* The number behind the conclusion was the follow- up time interval.

Table 3. Data combined with and without signal time curve

	Malignant	Benign	Total
MRI +	6	1	7
MRI -	2	13	15
Total	8	14	22

Sensitivity = 75%, Specificity = 92.8%, PPV = 85.7%, NPV = 86.6%, Accuracy = 86.4%

Table 4. Data without signal time curve

	Malignant	Benign	Total
MRI +	3	1	4
MRI -	2	4	6
Total	5	5	10

Sensitivity = 60.0%, Specificity = 80.0%, PPV = 75.0%, NPV = 66.6%, Accuracy = 70.0%

Table 5. Data without signal time curve

	Malignant	Benign	Total
MRI +	3	0	3
MRI -	0	9	9
Total	3	9	12

Sensitivity = 100.0%, Specificity = 100.0%, PPV = 100.0%, NPV = 100.0%, Accuracy = 100.0%

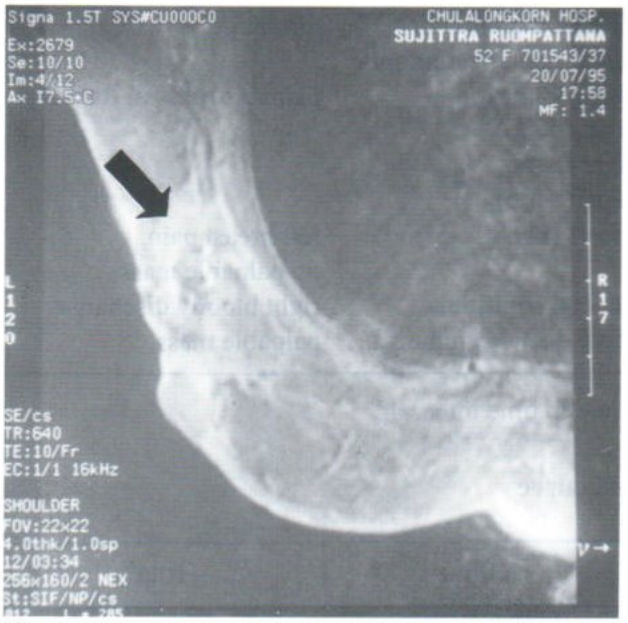


Fig. 1. Contrast MRM of right breast (T1WI with fat suppression) in axial view showed an irregular mass with rim enhancement (arrow), classified as malignant morphology

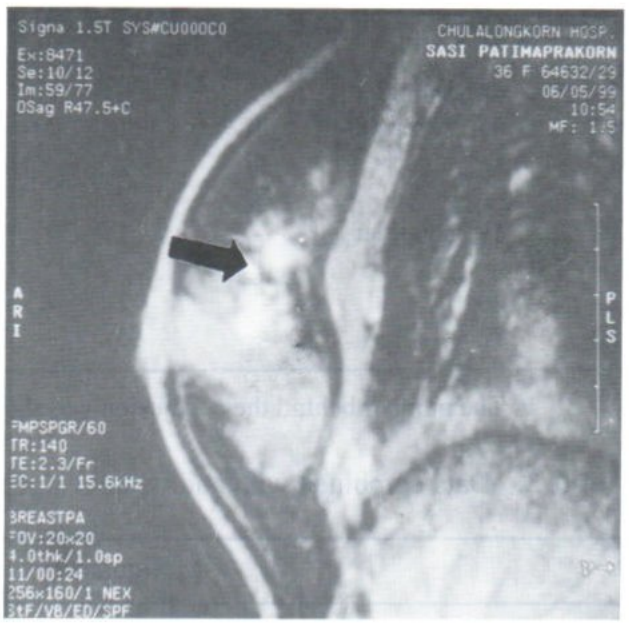
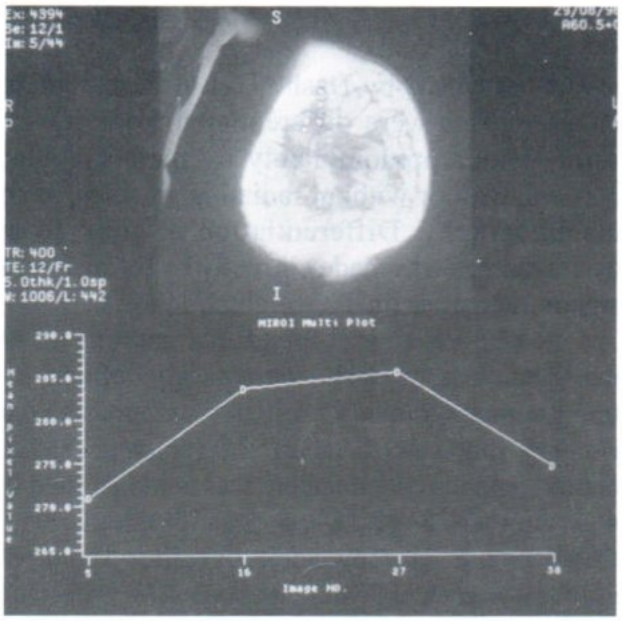
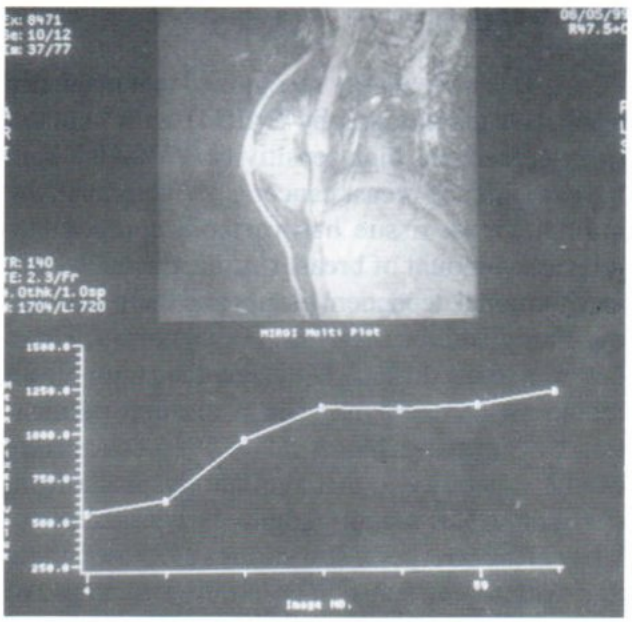


Fig. 2. Contrast MRM of right breast (T1WI with fat suppression) in sagittal view showed irregular lesion with heterogenous en hancement (arrow), classified as malignant morphology

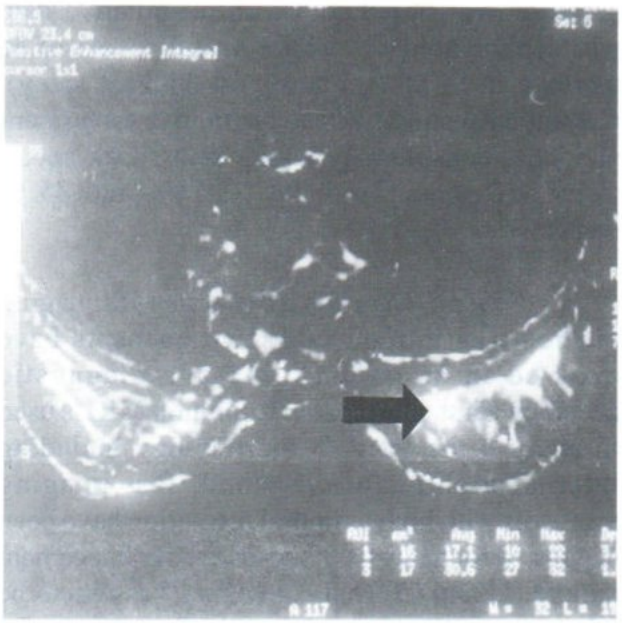


3A

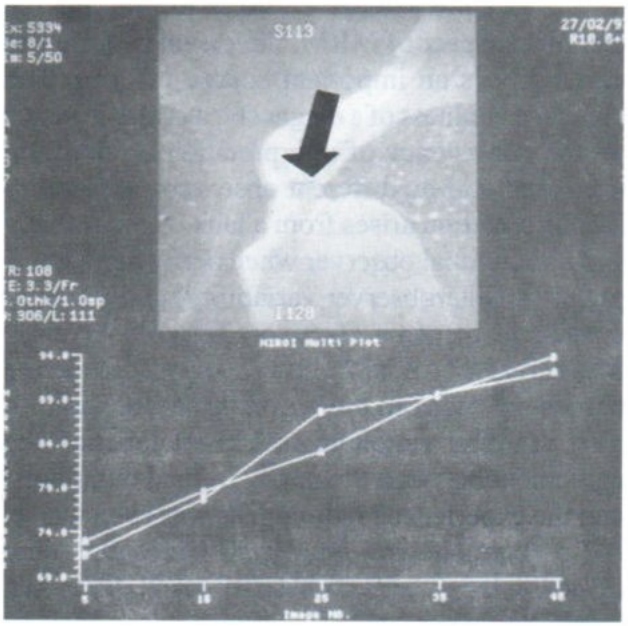


3B

Fig. 3 A,B. Contrast MRM with dynamic study showed washout signal time curve, type I (Fig.3 A), and plateau signal time curve type II (Fig. 3 B)



4A



4B

Fig. 4A. Contrast MRM with subtraction in axial view showed a well defined homogenous hypersignal intensity mass in left breast (arrow), classified as benign morphology

Fig. 4 B. Contrast MRM with dynamic study showed a spiculated lesion (arrow) with type I signal time curve, classified as probably benign lesion (MRI score = 2)

DISCUSSION

It is now widely recognized that magnetic resonance mammography (MRM) with contrast enhancement has high sensitivity (93%-100%) in the detection of breast cancer.[2,10,11,12] Because the normal breast tissue has variable components related to amount of breast stroma, ductal system and hormonal dependent tissues and there are various fibroglandular patterns in each woman. These factors make it difficult to differentiate tumor from the breast parenchyma.[6] Since the first publication by Heywang SH. et al.[6] in 1986 concerning MRI's capability to differentiate dysplasia from carcinoma, MR mammography has gained popularity in the past years and various MRI sequences and techniques have been studied to improve diagnostic accuracy.[4,14-17] This capability is based on the fact that all carcinomas enhanced whereas dysplastic tissue enhanced slightly or not at all after Gd-DTPA injection.

Despite extensive efforts to improve the technical aspect of MRM, the extent of observer variability is an important source of error. The clinical usefulness of a diagnostic test also depends on the consistency of interpretation on different occasions and by different observers. Variability in interpretation arises from a lack of consistency by an individual observer when performing interpretation (interobserver variability) and a lack of consistent between observers (interobserver).[18] Mussurakis S. et al[18] showed only a moderate agreement between the two experienced radiologists in rating morphological characteristics, the agreement between the newly trained radiologist and the experienced radiologists was even worse. All readers showed good sensitivity in cancer detection but specificity was substantially lower.

MRM provides excellent anatomy and tissue morphology by using T1 and T2 weighted images. Including dynamic contrast study, MRM helps to clarify the tissue characteristics. Many reports have described the MRI features of benign and malignant lesions.[19-22] In the early reports of MRM by Dash N. et al.,[21] malignant breast masses were differentiated from benign solid lesions predominately by their irregular borders, with or without radiating spicules, as in mammography. Differentiation of solid from cystic masses was made correctly by the different signal intensities on T2 weighted images.[8]

LIU PF. et al.[17] found that margins of 44 malignant lesions (64%) were poorly defined, 25 malignancies showed well define borders. An irregular shape was found in 55 carcinomas (80%). Heterogeneous enhancement was demonstrated in 44 lesions (64%), and 8 lesions (12%) showed rim enhancement. Homogeneous or diffused contrast uptake was seen in 17 malignancies. They reported the sensitivity and specificity for the identification of breast cancer by MRM when based on qualitative morphological analysis alone were 83% and 54%. However the diagnostic accuracy of 71% was lower than that achieved when interpretation was based solely on quantitative data with a threshold of 90% (cut-off levels of % increase in SI at 1 minute post-contrast study). Combined quantitative and qualitative assessment yielded a considerably higher sensitivity, specificity and accuracy of 93 %, 74% and 85 % respectively.

Several years ago a dynamic MR imaging method was introduced.[12] Two concepts have evolved in attempt to improve diagnostic accuracy. First, high spatial resolution MRI is used to analyze the lesion's morphology including internal architecture. Second, fast imaging protocols with high temporal resolution have been suggested for analysis of the lesion's enhancement pattern.[14] Kuhl CK and colleagues[14] assessed the relevance of the signal intensity time course for the differential diagnosis of enhancing lesions in dynamic MR imaging of the breast. They studied 101 malignant and 165 benign lesions and found that the distribution of the curve types for breast cancers was type I, 8.9%; type II, 33.6%; and type III, 57.4%. The distribution of curve types for

benign lesions was type I, 83.0%; type II, 11.5%; and type III, 5.5%. The diagnostic indices for signal time curve were, sensitivity, 91%; specificity, 83%; and accuracy, 86%. They concluded that a type III time course is a strong indicator of malignancy and is independent of other criteria.

In our series, by using the MRI score as the parameter for establishing the diagnosis, the sensitivity, specificity and accuracy were 75.0%, 92.8% and 86.4% respectively. Furthermore, the lesions that we interpreted were analyzed into two groups; group I with signal time curve and group 2 without signal time curve. The sensitivity, specificity and accuracy were 60.0%, 80.0% and 75.0% in group I, 100%, 100% and 100% in group II, respectively. According to our one false positive case and two false negative cases in group I, there were only qualitative images. The dynamic study, subtraction images and SI-time curve were not performed at that time. We had found the difficulty in differentiation of malignant and benign lesions using only morphological qualitative images because the features between the benign and malignant lesions were overlapping and the diagnostic criteria for achieving optimal results were poorly defined. Consequencely, the signal time curve helped to distinguish the lesion precisely. Of the twelve lesions with signal time curves, five benign lesions were type I, two malignant lesions were type III. For the type II, there were three benign and one malignant lesions. Our study was concordant with Kuhl CK. and collegues[14] that type I indicated benignity and type III indicated malignancy. Since the type II could be presented in both benign and malignant lesions, combination of the MRI morphology and pattern of enhancement were necessary to judge the diagnosis.

In conclusion, contrast enhancement MRM with morphologic features and patterns of enhancement play important role in distinguishing the benign from malignant breast lesions that are indeterminated by mammography and ultrasonography. In our study, by adding the dynamic contrast study and signal time curve give not only confidence in diagnosis but also increase in sensitivity and specificity.

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