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A comparison of imaging methods in the evaluation of breast pathologies

Meme patolojilerinin değerlendirilmesinde görüntüleme yöntemlerinin karşılaştırılması

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Abstract
Evaluating the performance of magnetic resonance imaging (MRI) and comparison with mammography, ultrasound (US) and histopathology results in cases of women with suspicious breast lesions. Forty nine cases on which histopathology was performed included in the study. All cases were applied mammography and US, and then MRI. Biopsy or post-operational results have been generated. Among the 49 cases, 27 (55%) benign and 22 (45%) were malign lesions. Using mammography, of the 49 cases, 24 (49%) were deemed to be malign. True positive cases were 20 (41%). In ultrasound, 25 (51%) were malign, 24 (49%) were benign. True positive cases were 21 (43%). Lesions were detected in all of the 49 cases using MRI. All of the 22 (45%) malign cases were diagnosed as malign lesion. Sensitivities of mammography, US and MRI in detecting lesions were 83%, 95% and 100%, and specificities were 85%, 85% and 92% respectively. In MRI, all cases were applied dynamic contrast sequences, for the cases with lesions detected, time signal intensity (SI) curves were drawn. 23 cases were detected as Type 1 (47%), 2 cases were Type 2 (4%), 24 cases were Type 3 (49%) SI curve. According to SI curves sensitivity in detecting malignities was 95% and specificity was 81%. MRI has been found superior to mammography and US in detecting masses especially with its characteristics of higher spatial resolution, less binding of dynamic properties evaluation on user. There may be a decrease of unnecessary interventional operations in benign-malign detection of breast lesions using dynamic breast MRI.
Keywords: Breast; magnetic resonance imaging; mammography; ultrasound

Özet
Şüpheli meme lezyonu olan olgular mamografi, ultrasonografi (US) ve manyetik rezonans görüntüleme (MRG) yöntemi ile değerlendirilerek, histopatolojik sonuçları ile karşılaştırılmıştır. Histopatolojik incelemesi yapılan yapılan 49 olgu çalışmaya alındı. Tüm olgulara öncelikle mamografi ve US, daha sonra MRG uygulandı. Biyopsi veya ameliyat sonrası histopatolojik sonuçlar elde edildi. Patolojik sonuçlara göre 49 olgunun 27 (%55) tanesi benign, 22 (%45) tanesi malign lezyondu. Mammografi ile 49 olgunun 42 (%85) tanesi saptanabildi. Mamografi ile 49 olgunun 24 (%49) tanesi malign olarak değerlendirildi, bunlar arasında gerçek pozitiflerin sayısı 20 (%41) idi. Ultrasonografi ile 49 olgudaki lezyonların tamamı saptandı. 25 (%51) olgu malign, 24 (%49) olgu benign olarak değerlendirildi. Gerçek pozitif olgu sayısı 21 (%43) idi. MRG ile 49 olgunun tamamında lezyon saptandı. 22 (%45) malign olgunun tamamına malign lezyon tanısı konuldu. Memenin kitlesel lezyonlarını saptamada mamografi, US ve MRG'nin sırasıyla sensitivitesi %83, %95 ve %100, spesifitesi ise %85, %85 ve %92 olarak bulundu. MRG'de tüm olgulara dinamik kontrastlı sekanslar uygulandı, kontrastlanma şekilleri ve hızları değerlendirildi, lezyon saptanan olgulara zaman sinyal intensite (SI) eğrileri çizdirildi. 23 olguda Tip 1 (%47), 2 olguda Tip 2 (%4), 24 olguda ise Tip 3 (%49) SI eğrisi olarak saptandı. Tip 1 eğrinin benign, Tip 2 ve 3 eğrinin olası maligniteleri gösterdiği kabul edildi. Bu verilere göre zaman/sinyal intensite eğrilerinin maligniteleri saptamada sensitivitesi %95, spesifisitesi %81 olarak saptandı. MRG özellikle uzaysal çözünürlüğün daha yüksek olması, dinamik özelliklerin değerlendirilmesinin kullanıcıya daha az bağımlı olması, özellikleri ile kitleleri saptamada mamografi ve US'ye oranla daha üstün olarak bulunmuştur. Meme MRG ile dinamik inceleme kullanılarak meme lezyonlarının benign-malign ayrımında gereksiz girişimsel işlemlerin sayısında azalma sağlayabileceğini düşünmekteyiz.
Anahtar kelimeler: Meme; manyetik rezonans görüntüleme; mamografi; ultrasonografi

Introduction

Mammography is the primary screening method in the detection of breast cancer. The sensitivity of mammography ranges from 69% to 90%, and its specificity from 54% to 69% (1,2). Although it is a study with a high sensitivity, it has a low degree of reliability in patients with dense breasts, dysplastic diseases and breast implants, as well as in patients evaluated after breast operation or radiotherapy. Because its specificity is not sufficiently high, biopsies based on mammography give benign results to a significant degree (75%) and one in every four female patients with a suspicious breast lesion undergoes an unnecessary biopsy (3,4).

Ultrasonography (US) is a useful and informative method in detecting palpable lesions, in differentiating cystic and solid structures, and in classifying the lesions. However, microcalcifications such as those in ductal carcinoma in situ (DCIS) are frequently difficult to view with US (4).

Magnetic resonance imaging (MRI), on the other hand, is an efficient method with its supremacy in soft tissue resolution, specialty of multiplanar imaging and its being free of ionizing radiation use (4).

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In this study, mammography, US and MRI findings are compared with histopathological results and their role in establishing a diagnosis is evaluated in the light of current literature.

Material and Methods

From among the patients presenting with a breast mass at the Radiodiagnostic Department between September 2007 and February 2009 and given mammography and ultrasound followed by MRI, a total of 49 cases who underwent subsequent histopathological examination were taken into the present study. All three imaging methods were reviewed separately and independently by three radiologists and all data obtained were compared with the pathological results. Written consent was obtained from all the patients recruited. Patients without a histopathological diagnosis were excluded.

Mammographic examinations were made using a Siemens mammography machine (Mammomat 3000; Siemens Medical Systems, Erlangen, Germany). Views were taken routinely as craniocaudal (CC) and mediolateral-oblique projection. Single emulsion 18x24 film was used in mammagraphic imaging, opting for 24x30 cm film for larger breasts.

Ultrasonographic examinations, using the Siemens Acuson Anteres (Siemens AG Wittelsbacherplarz Muenchen Germany) ultrasonography machine, were performed sychronously with the mammography examinations with a 7.5-13 MHz linear probe.

MRI scans were taken with the 1.5 Tesla MR (Phillips Gyroscan Intera, Netherlands) machine, using the approriate breast coil. In the primary stage, T1-weighted spin-echo (SE) (TR/TE 500/4,6), T2-weighted TSE (FS) and fat-suppressed T2A sequences in an axial plane were taken to define the localization of the lesion and its morphology without contrast. The parameters of the sequences used were as follows: flip angle (FA) 30º, slice thickness 3 mm ve matrix 128x256. Following pre-contrast images, contrast material gadopentate dimeglumine (Gd-DTPA) 0.2 mmol/kg was administered as bolus injection by hand. In the dynamic study, following an imaging series without contrast, during the 30 seconds waiting period set automatically by the machine, i.v. contrast was injected in a rapid manner and the area was viewed six times in quick succession. At the end of the examination, to make contrast enhancement more prominent, subtraction procedure was performed in patients in whom motion artifact was impeded following the contrast injection. Early and late contrast slices were subtracted from those without, slice by slice, and subtraction images were obtained. Thus, enhanced tissue was differentiated from fat. Kinetic analysis was effected at a time when enhancement was the fastest and most prominent during the six successive imagings. The fastest and most strongly enhanced area of the suspected lesion (ROI: region of interest) was calculated and the time-signal intensity curves were obtained.

Mammography, US and MRI findings were evaluated independently of one another. The characteristics for these imaging methods were decided on in accordance with the American College of Radiology criteria BIRADS. The contour, homogenity and calcification of the lesion were evaluated in the mammography. Contour irregularity, spiculation, heterogeneity and microcalcification, breast skin thickening, and microlobulation were chosen as the criteria for suspected malignancy.

In the ultrasound examination, differentiation of cyctic and solid lesions was paid special attention. Contour characteristics, echogenity, calcification and the posterior echo of the lesions were evaluated. In the MRI examination, evaluation was directed at the morphological and dynamic characteristics of the lesions. As far as the morphological features were concerned, skin thickening, irregular or bad-looking borders, spiculated contours, existence of microlobulations, and also an enhancement pattern which was peripheral or of rim, ductal, linear or clumped shape were interpreted as suspicious for malignancy.

In enhanced imagings, the time of enhancement (early or late) and the enhancement pattern were evaluated. Lesions with late and homogenous enhancement were considered to be benign, and those with early, heterogenous, peripheral or halo-type enhancement were considered to be malignant. Following the study by Buadu et al. (5), time-signal intensity (SI) curves were classified under four different types, depending on the washout characteristics of the contrast material. These were: Type 1a (continuously increasing enhancement), Type 1b (continuously increasing curve enhancement), Type 2 (plateau), and Type 3 (washout).

Statistical sensitivity, specificity, positive predictive and negative predictive values and accuracy rates for these three modalities were determined. Further, the time-signal intensity curves obtained in all the MRI scans were compared with the pathology results.

Statistical analysis:

Sensitivity = patients with suspected breast cancer/patients with histologically confirmed breast cancer

Specificity = patients with suspected benign disease/patients with histologically confirmed benign disease

Positive predictive value = patients with histologically confirmed breast cancer/patients with suspected breast cancer

Negative predictive value = patients with histologically confirmed benign disease/patients with suspected benign disease

Accuracy = patients with true-positive and true-negative detected disease/patients with histologically confirmed breast cancer

Results

A total of 49 patients, aged 21-79, were taken into the study. Forty eight (98%) of these patients were female, and 1 (1%) was male. Pathological study revealed lesions that were benign in 27 (55%) patients and malignant in 22 (45%). The commonest lesion found was fibroadenoma (Table 1, Figure 1a-c). The commonest malignant lesion, on the other hand, was found to be invasive ductal adenocarcinoma (Table 2, Figure 2a-c).

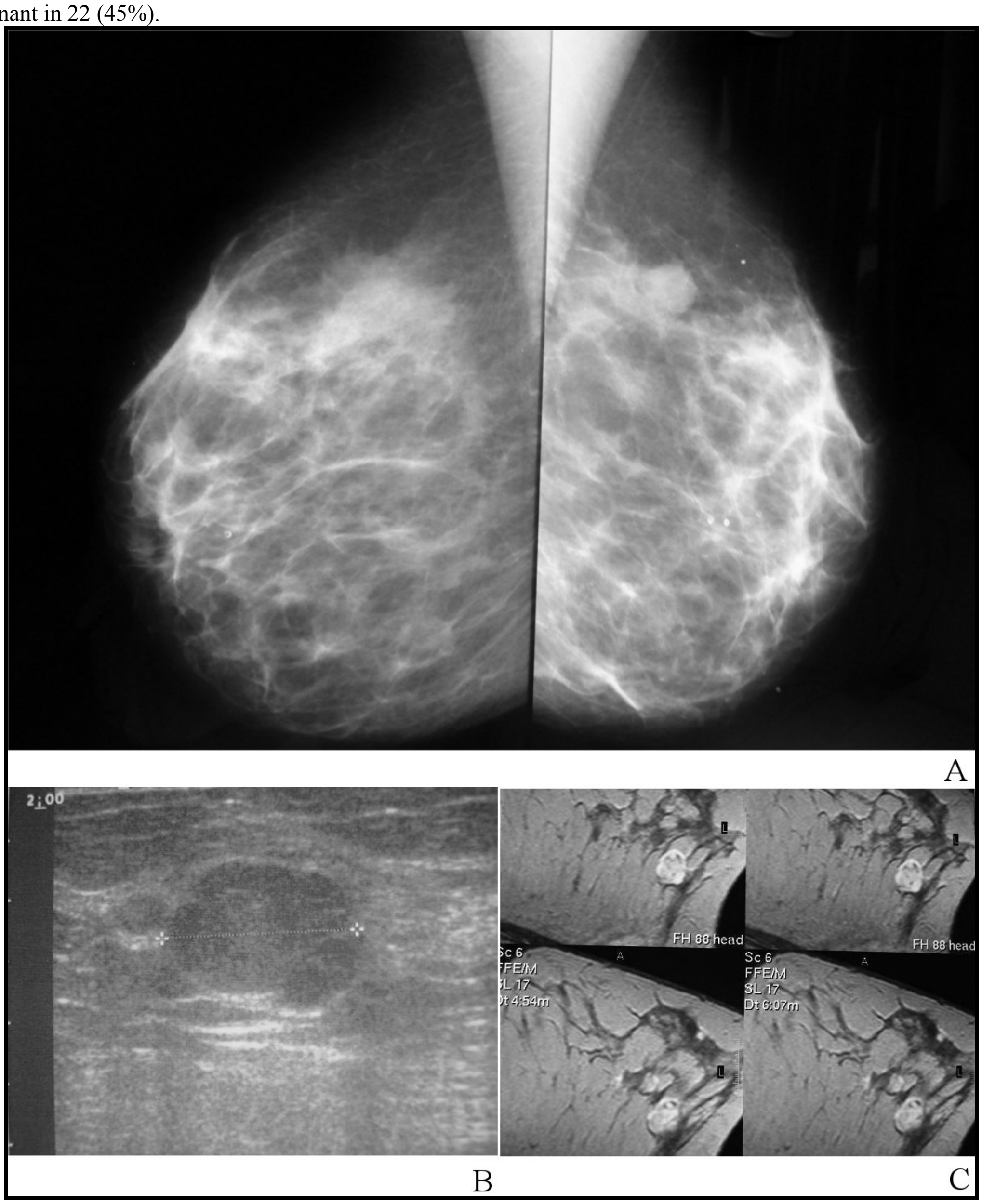

Figure 1. (a) 35 years old woman with history of fibroadenom in the upper external quadrant of the left breast. Mammography shows nodular opacity with affected contours in the upper external quadrant of the left breast. (b) Gray-scale sonogram reveals hypoechoic solid lesion exhibiting one microlobulation. (c) T1-weighted post contrast axial MR images show non enhanced internal septation.

Table 1. Distribution of benign lesions.

Histopatology (Benign)	**Number of lesions**	**Percent**
Fibroadenoma	10	37
Fibrocystic disease	7	26
Inflammation	3	11
Adenofibrosis	2	9
Other (intraductal papillamatosis, cyst hydatic, hamartoma, fibrous scar andfat necrosis)	5	18
Total	27	100

Table 2. Distribution of malign lesions.

Histopatology (Malign)	Number of lesions	Percent
Invazive ductal carcinoma	18	81
DCIS	2	9
Invazive papillary carcinoma	1	5
Invazive lobular carcinoma	1	5
Total	22	100

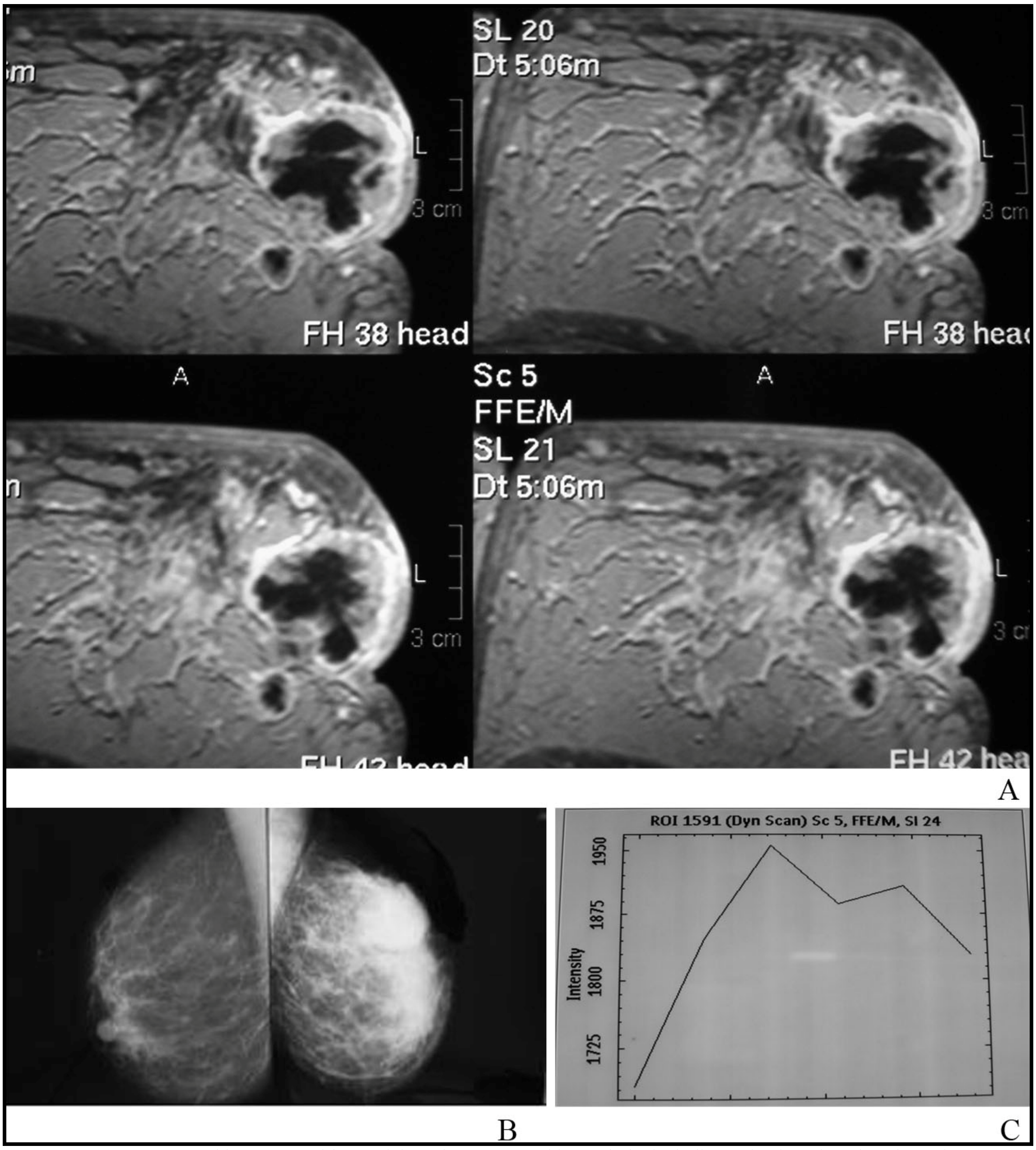

Figure 2. (a) 52 years old woman with suspicious breast mass histopathological diagnosis: invasive ductal carcinoma. (a) Mammography shows asymmetrical nodular density increase with slightly irregular borders, and thickened breast skin in the upper external quadrant of the left breast. (b) T1-weighted post contrast axial MR images show periferal ringlike enhancement starting from first second. (c) Time signal-intensity curve: Type 3.

With conventional mammography, we were able to detect 42 (82) of the 49 lesions. 7 (15%) cases went undetected. Of the 42 lesions detected, 24 (57%) were evaluated as malignant, and 18 (43%) as benign. 2 (4%) of the lesions that went undetected were malignant and 5 (10%) were benign (Table 3). The lesions undetected by mammography had a pattern of sclerosing (Type 3-4) breast lesion. In view of the results obtained, the sensitivity of mammography was found to be 83%, its specificity 85%, positive predictive value 83%, negative predictive value 92%, and the rate of accuracy 87% (Table 4).

Table 3. Comparison of the mammography (MG), US and MRI diagnoses based on the pathological results.

Histopatology	Mammography			US		MRI		MG+US		MG+MRI	
	Benign	Malign	Normal	Benign	Malign	Benign	Malign	Benign	Malign	Benign	Malign
Benign	18	4	5	23	4	25	2	23	4	25	2
Malign	0	20	2	1	21	0	22	1	21	0	22
	18	24	7	24	25	25	24	24	25	25	24

Table 4. Comparison of the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy ratio of MG, US and MRI based on the pathological results.

	Sensitivity%	Specificity%	PPV %	NPV %	Accuracy Ratio%
MG	83	85	83	92	87
US	95	85	84	84	89
MRI	100	92	91	1	95
MG+US	95	85	84	84	89
MG+MRI	100	92	91	1	95

Table 5. Dynamic properties.

	Time-signal intensity (SI) curves		
	Type I	Type II	Type III
Benign	22 (44.8%)	2 (4.2%)	3 (6.3%)
Malign	1 (2.1%)	0	21 (42.6%)

With ultrasonography, we were able to detect all of the lesions that our 49 cases presented. 25 (%51) cases were evaluated as malignant and 24 (%49) cases were evaluated as benign. In comparison with the histopatological results, 4 (8%) cases were found to be false positive and 1 (2%) was found to be false negative. Of these 4 (8%) cases, 2 (4%) were diagnosed as fibroadenoma, 1 (2%) as adenofibrosis, and 1 as fibrocystic disease. The 1 (2%) false negative result was pathologically diagnosed to be that of invasive ductal carcinoma. The sensitivity of ultrasonography was thus found to be 95%, its specificity 85%, positive predictive value 84%, negative predictive value 84%, and the rate of accuracy 89% (Table 4).

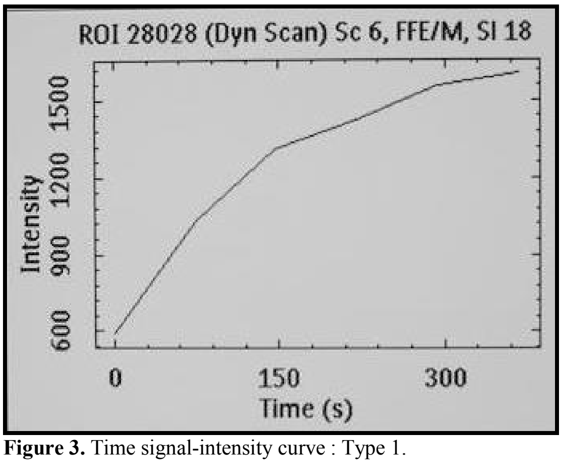

Figure 3. Time signal-intensity curve : Type 1.

With MRI, the lesions were detected in all of the 49 cases. All 22 (45%) cases of malignancy were detected as malignancy; and the number of false positive cases in 27 (55%) benign cases was 2 (4%) (Table 3). Histopathological results revealed one of these two to be a case of fibroadenoma and the other of adenofibrosis. The sensitivity of MRI was thus found to be 100%, its specificity 92%, positive predictive value 91%, negative predictive value 100%, and the rate of accuracy 95% (Table 4).

When mamography and ultrasonography were evaluated in combination, 24 (49%) cases were evaluated as benign, and 25 (51%) as malignant. 1 (2%) case received a false negative diagnosis, the lesion going undetected in mammography and being mistaken for fibrocyctic disease in ultrasonography. It was subsequently diagnosed as invasive ductal carcinoma in the histopathological examination. The sensitivity and specificity of this combined application bore resemblance to those of ultrasonography alone (Table 3,4).

When mamography and MRI were evaluated in combination, all of the malignant cases were detected. 2 (4%) of the benign cases received a false positive diagnosis; histopathological examination revealed one to be a case of fibroadenoma and the other of adenofibrosis. In view of these results, the highest sensitivity and specificity rates were obtained by MRI alone or by mamography and MRI in combination (Table 3,4).

Of the time-signal intensity (SI) curves applied to the 49 cases that showed enhancement in MRI, 23 (48%) were Type 1 SI curve, 2 (4%) were Type 2, and 24 (50%) were Type 3 (Figure 3). Only 1 (2%) case was malignant in the Type 1 curve group and this was a case of invasive ductal carcinoma. The remaining 22 (45%) in this group were benign cases. The 2 (4%) cases in the Type 2 group were also evaluated as benign; one of these was fibroadenoma and the other was a fibrocyctic change. Of the cases in whom a Type 3 curve was detected, 3 (6%) were benign and 21 (43%) were malignant. The 3 (6%) benign cases were evaluated as fibroadenoma, inflammation and adenosis (Table 5). These findings were compared with the histopathological results. For statistical analyses, it is accepted that Type 1 curve denotes benign cases and Type 2 and 3 curves denote probable malignancy. According to our data, when time-signal intensity curves are compared with histopathological results, their sensitivity is 95%, specificity 81%, positive predictice value 77%, negative predictive value 95%, and the rate of accuracy is 87%.

Discussion

When imaging modalities of mammography, ultrasonography and MRI were compared with one another, the sensitivity and specificity of MRI in establishing a diagnosis was found to be superior to those of the other two.

The primary target of the imaging methods applied in diseases of the breast is the detection of breast cancer. Mammography is an efficient scanning method for early-phase breast cancer detection (6). But, there are certain limiting factors to its capacity to make accurate diagnosis. The most limiting circumstance is when the case presents a dense breast pattern. The sensitivity of mammography is decreased down to the levels of 30-48% in dense breast cases. Thomas et al demonstrated in a study that the sensitivity of mammography varies according to age, breast density, and hormonal factors, but the most important among them is breast density (7,8). High-risk cases are more commonly seen among the young and the sensitivity of mammography here is even more limited. Because the frequency of dense breast decreases with age, the sensitivity of mammography is greater in higher age groups (8,9). The 2 invasive ductal carcinoma cases in our study, too, which went undetected in mammography, had a strongly dense parenchyma characteristic. The fact is that mammography is not efficient enough in detecting lesions in the dense breast pattern and this circumstance is independent of the patients' age (6,10).

Ultrasonography is quite a useful method in differentiating cyctic lesions from the solid ones. Furthermore, it is an efficient guide in the percutaneous biopsy of solid lesions and in the aspiration of cystic lesions. High-resolution ultrasonography, especially, is of great use in characterizing certain lesions detected by mammography and in determining the lesion dimensions. On the other hand, ultrasonography has certain limitations in bilateral breast cancer, in cases with intraductal spread and in detecting multifocal lesions (11). Houssami et al. (12) found the sensitivity of ultrasonography to be 80,5% in patients given mammography in correlation with ultrasonography. In our study, the sensitivity of ultrasonography was found to be 95%. One case was diagnosed with ultrasonography as fibrocystic disease since it displayed a regular border and a cyctic character. The patient did not have a palpable lesion and only the MRI findings suggested a malignancy. The histopathological examination of this patient revealed it to be invasive ductal carcinoma.

Another method of diagnosis in evaluating breast disease is MRI. Although MRI is not the primary imaging method in scanning for breast cancer, it is employed as a complement for the conventional breast imaging methods and as a problem solver. Breast MRI with enhancement has reached a level of sensitivity of up to 100% in diagnosing invasive breast cancers and a level ranging from 40% to 100% in DCISs. The probable reasons for this wide range of sensitivity are thought to be the small-size study groups, use of different study techniques, and histological differences (13). The sensitivity of MRI in our study was found to be 100% and thus was in keeping with the level reported in literature. Two cases diagnosed histopathologically as DCIS were evaluated as malignant with their morphological and dynamic properties in the MRI examination. It has been reported that breast MRI sensitivity in detecting DCIS is lower than that in detecting invasive carcinomas when breast lesions are evaluted individually, and the reason is suggested to be the fact that microcalcifications detected by mammography cannot be viewed in MRI, the fast enhancement of the lesions in the DCIS phase of the tumor (due to incomplete angiogenesis), and a lack of washout observation (14).

Malur et al. (15), however, while reporting a higher sensitivity for MRI in detecting ductal carcinomas in comparison with US and mammography, stated that MRI has a lower sensitivity than the combined use of mammography and US. Not with standing, we found higher levels of sensitivity and accuracy for MRI in comparison with mammography or with mammography combined with ultrasonography.

In our study, one case was histopathologically diagnosed as invasive lobular carcinoma (ILK). ILK accounts for less than 10% of all breasts cancers. In US and mammography, though not particularly distinctive, it may sometimes be seen as a focal mass, calcification or a form of asymmetry. Studies show that MRI is more effective than the conventional methods in diagnosing ILK and that it increases the rate of detecting multifocal tumors (16). However, Yeh et al. (17) reported that the enhancement patterns are not viewed as they are in classic malignancies, because ILK can grow without angiogenesis and neovascularization, and therefore false negative results are obtained. In our study, too, the suspected lesion was demonstrable with US and mammography findings. On the other hand, the fact that in MRI the lesion quickly enhanced in the early phase, had a washout, and the time SI curve was in accordance with Type 3 supported the diagnosis. Especially in lobular carcinoma, ductal carcinoma in situ and some types of invasive carcinoma, benign kinetic curves may be obtained due to weak angiogenetic activity. This, leads to false negative results (18,19).

In our study, time-signal intensity curves were considered to be important parameters in differentiating benign and malignant lesions. They were even treated as a guide to differential diagnosis. The curves obtained were compared with the histopathological results. For statistical analysis, it was accepted that curves showing a plateau and washout (Types 2 and 3) were associated with malignancies, and those continuously rising (Type 1) with benign lesions. According to these data, the sensitivity of the time-signal intensity curves was found to be 95%, their specificity 81%, positive predictive value 77%, negative predictive value 95%, and their rate of accuracy 87%. This shows a parallelism to the values for sensitivity (91%), specificity (93%), and rate of accuracy (37%) as quoted in the literature (18).

However, one case evaluated as Type 1 was diagnosed in the histopathological examination as invasive ductal carcinoma, and 5 cases evaluated as Types 2 and 3 curves were diagnosed as fibroadenoma and inflammation. A number of reasons are posited for this occurence. First of all, pertaining to imaging techniques, if post-contrast images in low temporal resolution situations are taken only after the highest point of enhancement, the washout may be missed. Another factor is the failure to observe the enhancement washout in cases of biologically or pathologically reduced vein density or of arteriovenous anastomosis. In premenopausal patients, quick enhancement of parenchyma of the neighbouring breast in a similar way as with the lesion may mask malignancies (20).

Combined use of MRI and mammography has been a breakthrough in the characterization of lesions as it is a noninvasive method of great efficacy. The fact that MRI has a high accuracy rate in detecting malignancies in suspected breast lesions suggests that need for biopsy may become reduntant in some cases, thus leading to a noninvasive approach as was argued by Vassiou et al. (11), and our study indeed supports this assessment.

Primary usefulness of mammography in detecting breast lesions cannot be questioned, but in the characterization of malignant lesions the combined use of mammography and MRI is the most efficient noninvasive method. We suggest that, especially in suspected and indefinite breast lesions, making an MRI evaluation before proceeding to histopathologcal diagnosis is the preferable approach.

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