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Research Article

Subcentimeter Solid Breast Lesions with Suspicious Ultrasonographic and Benign Histopathological Features: Sonographic Characterization

Sonografik Olarak Kuşkulu Olan ve Histopatolojik Olarak Benign Tanı Alan 1 cm'den Küçük Solid Meme Lezyonları: Sonografik Karakterizasyon

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Abstract

Aim: The aim of our study was to reveal the types and sonographic features of the margins in solid lesions less than 10 mm in dimension, considered suspicious for malignancy in breast ultrasonography, and histopathologically diagnosed as benign; and therefore, to recall the features that will facilitate the evaluation of radiology-pathology compatibility after biopsy.

Material and Methods: This study was conducted with 82 women, with BI-RADS 4-5 lesions sonographically, between 2017 and 2020. Lesion size and margins, presence of posterior shadowing and microcalcifications were scanned retrospectively. Lesions were classified according to their margins as smooth-macrolobulated, microlobulated, irregular-indistinct, angular and spiculated.

Results: Histopathologically, the most common benign lesions were fibroadenoma (n=26, 31.7%) and fibrocystic changes (n=15, 18.3%). Sonographically, the mean size of the lesions was 8.96±1.46 mm, and the most common margins were irregular-indistinct in 39%, and smooth-macrolobulated in 30%. In the statistical analysis, the incidence of fibroadenoma was found to be significantly higher in the BI-RADS 4a group compared to the patients in the other pathological diagnosis group (p:0.007).

Conclusion: In this study, it was concluded that the indistinct-irregular, microlobulated and angular margins could also be observed significantly in subcentimeter benign breast lesions, and as the size of the lesion got smaller, it becomes difficult to differentiate the features of the margins; hence they should be evaluated more carefully.

Keywords: Benign breast lesions, BI-RADS, sonographic margin, subcentimeter, ultrasonography

Öz

Amaç: Meme lezyonunun karakterini sonografik olarak değerlendirirken lezyon sınırları en önemli sonografik kriter olarak bilinir. Çalışmamızın amacı, meme ultrasonografi incelemesinde 10 mm ve daha küçük boyutlarda ölçülen ve malignite açısından kuşkulu değerlendirilen, histopatolojik olarak benign tanı alan solid lezyonların tiplerini ve sonografik kenar özelliklerini ortaya koymak; böylece biyopsi sonrası radyoloji-patoloji uyumunu değerlendirmeyi kolaylaştıracak özellikleri anımsamaktır.

Materyal ve Metot: 2017-2020 tarihleri arasında, sonografik olarak BI-RADS 4-5 olarak raporlanan 82 kadın olgu çalışmaya dahil edildi. Kitle boyutları ve kenar özellikleri, kitlede posterior gölgelenme ve mikrokalsifikasyon varlığı retrospektif olarak tarandı. Lezyonlar kenar özelliklerine göre düzgün-makrolobüle, mikrolobüle, düzensiz-belirsiz, açılı ve spiküle olarak gruplandırıldı.

Bulgular: Histopatolojik olarak en sık görülen benign lezyonlar fibroadenom (n=26, %31,7) ve fibrokistik değişiklikler (n=15, %18,3) dir. Lezyonların ortalama sonografik boyutu 8,96±1.46 mm ve sonografik kenar özellikleri %30'unda düzgün-makrolobüle, %12,2'sinde mikrolobüle, %39'unda düzensiz-belirsiz , %15,9'unda açılı ve %2,4'ünde spiküle idi. BI-RADS kategorisine göre lezyonların 48'i (%58,5) 4a, 29'u (%35,4) 4b, 3'ü (%3,7) 4c ve 2'si (%2,4) 5 olarak sınıflandırılmıştır. İstatistiksel analizde ise BI-RADS 4a grubunda fibroadenom olma oranı diğer patolojik tanı grubundaki olgulardan anlamlı düzeyde yüksek bulunmuştur (p:0.007).

Sonuç: Bu çalışma ile 10 mm ve daha küçük benign meme lezyonlarında da kaydadeğer oranda düzensiz-belirsiz, mikrolobüle ve açılı kenar özelliklerinin görülebileceği, lezyon boyutları küçüldükçe kenar özelliklerinin ayrımının zor olduğu ve daha dikkatli değerlendirilmesi gerektiği sonucuna ulaşılmıştır.

Anahtar Kelimeler: Benign meme lezyonları, BI-RADS, sonografik kenar, subsantimetre, ultrasonografi

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INTRODUCTION

Ultrasonography (US) is the most important additional modality today with high sensitivity and complementary to mammography for imaging breast lesions, since it is easily accessible, reproducible, inexpensive, and can be measured in multiple planes (1). US was previously used to distinguish between cystic and solid; however, its spectrum has expanded nowadays to make the distinction between benign and malignant, thanks to the additionally defined sonographic features as well as its internal nature (2).

With the technological advancements in screening programs and imaging, an increasingly important part of newly diagnosed cases of breast cancer consists of women with tumors of 10 mm or smaller (3,4). Small lesions are generally non-palpable, and they are more difficult to analyze with imaging methods compared to large lesions (5). Therefore, it is important to perform the characterization of these lesions accurately in order to increase detection rates of early breast cancers with a good prognosis or to reduce the number of unnecessary biopsies performed for benign lesions.

The margin of the lesion is known as the most important sonographic feature when evaluating the character of the breast lesion. Microlobulated, angular or spiculated margin, presence of microcalcification, prominent hypoechogenicity, posterior shadowing and vertical growth are signs in favor of malignancy, while the ellipsoid shape, macrolobulation, smooth margin, marked hyperechogenicity are considered as benign findings (6,7). On the other hand, it is known that the sonographic features of benign and malignant lesions may overlap.

There are many studies on the sonographic margin features of breast lesions in the literature. However, although there are few magnetic resonance imaging (MRI) studies evaluating subcentimeter breast lesions, there are very few ultrasonography studies describing lesions margin features (8-11). In this study, we aimed to identify the types and sonographic margin features of solid lesions measured as 10 mm and smaller in breast ultrasonography, considered suspicious for malignancy, and histopathologically benign; and to recall the features that will facilitate the evaluation of radiology-pathology compatibility after biopsy.

MATERIAL AND METHOD

This study was planned retrospectively, was checked for compliance with the Helsinki Declaration of Human Rights and was approved by the ethics committee of our hospital before the study (22.03.2021-107/14). The reports of the patients were analyzed, who presented to our breast department between 2017 and 2020 with various indications, who were diagnosed with solid masses of 10 mm or smaller with suspected malignancy in breast US, who underwent core biopsy and/or excision after US-guided stereotaxy. A total of 82 female patients with radiologically suspicious for malignancy but histopathologically diagnosed as benign were included in the study. The diagnosis was made by core needle biopsy in 49 patients, and by US-guided stereotaxy procedure in 19 patients. In 14 patients, surgical excision was performed after stereotaxy in addition to core biopsy due to radiological-clinical-histopathological discordance.

Breast US was performed with a 10-14 MHz linear probe (General Electric Medical Systems; Logic 6, Milwaukee, USA), and core-needle biopsy was performed using a 16 G (gauge) needle by a radiologist with minimum 10 years of experience. US scanning was performed in radial and anti-radial planes, and the longest dimensions of the lesions were measured in millimeters.

Lesions were classified according to the features of the margins specified in the Breast Imaging Reporting and Data System (BI-RADS) atlas as 1) smooth, 2) microlobulated, 3) indistinct-irregular, 4) angular, 5) spiculated (Figures 1-3). Lesions with macrolobulated margins were classified together with the smooth margin group. Findings with suspected malignancy such as microlobulated, indistinct-irregular, angular and spiculated margins were categorized as BI-RADS 4-5 (12). According to our current practice, lesions with suspicious margins in terms of malignancy, lesions with smooth /macrolobulated margins with increased size during follow-up, and lesions with heterogeneous internal structure and vascularity within the mass in doppler examination were considered suspicious, and biopsy and/or stereotaxic marking were performed for these lesions. In addition, the presence of cellular atypia and radiological-clinical-histopathological discordance after core biopsy were accepted as indications for surgical excision. When evaluating axillary lymph nodes, lymph nodes with more than 3 mm asymmetric or diffuse thickening, or obliterated fatty hilus were noted as suspicious for involvement (13).

According to histopathological diagnoses, the lesions were grouped as fibroadenoma, sclerosing adenosis, fibrocystic changes (cysts, adenosis, ductal hyperplasia without atypia, apocrine metaplasia), atypical ductal hyperplasia, intraductal papilloma, fat necrosis, inflammation-mastitis, radial scar, fibrosis and non-specific benign lesions (normal breast tissue, mature fat-connective tissue).

Male patients, patients below 18 years of age, patients whose US examination and pathological diagnosis from a remote site, lesions larger than 10 mm, lesions with intraductal localization, cystic masses and lesions reported as malignant as a result of pathology were not included in the study.

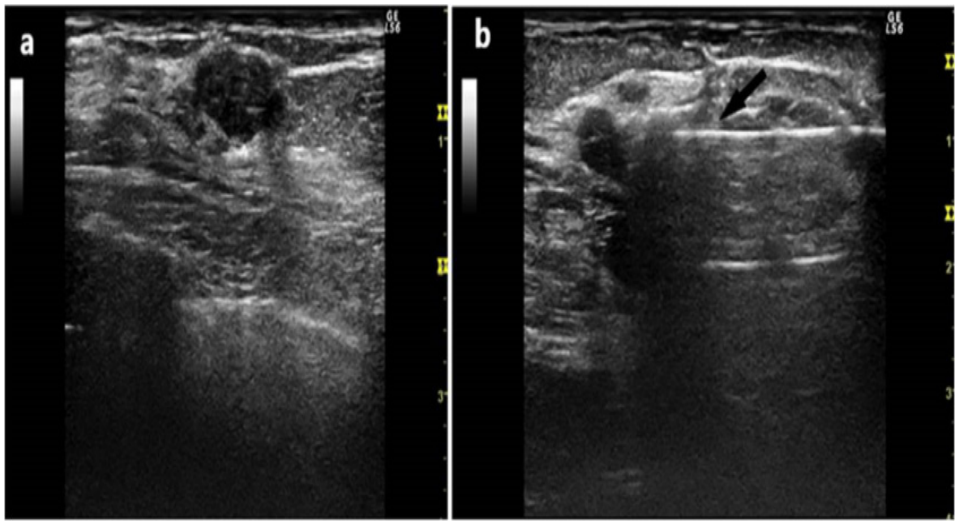

Figure 1. a) A 36-year-old woman with positive family history. US image shows a 10 mm hypoechoic mass with microlobulated margins. Histopathologic diagnosis was fibroadenoma. b) A 33-year-old woman. US image shows a 9.5 mm hypoechoic mass with microlobulated margins. Core needle biopsy image of the patient(arrow). Histopathologic diagnosis was fibrocystic changes

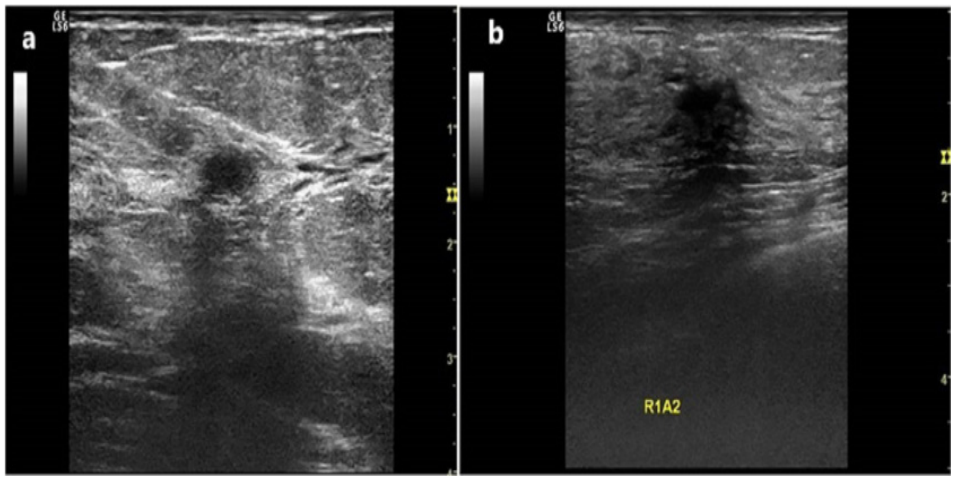

Figure 2. a) A 46-year-old woman. US image shows a 7.5 mm hypoechoic mass with indistinct-irregular margins. Histopathologic diagnosis was intraductal papilloma. b) A 68-year-old woman with positive family history. US image shows a 10 mm hypoechoic mass with indistinct-irregular margins and posterior acoustic shadowing. Histopathologic diagnosis was fibrosis

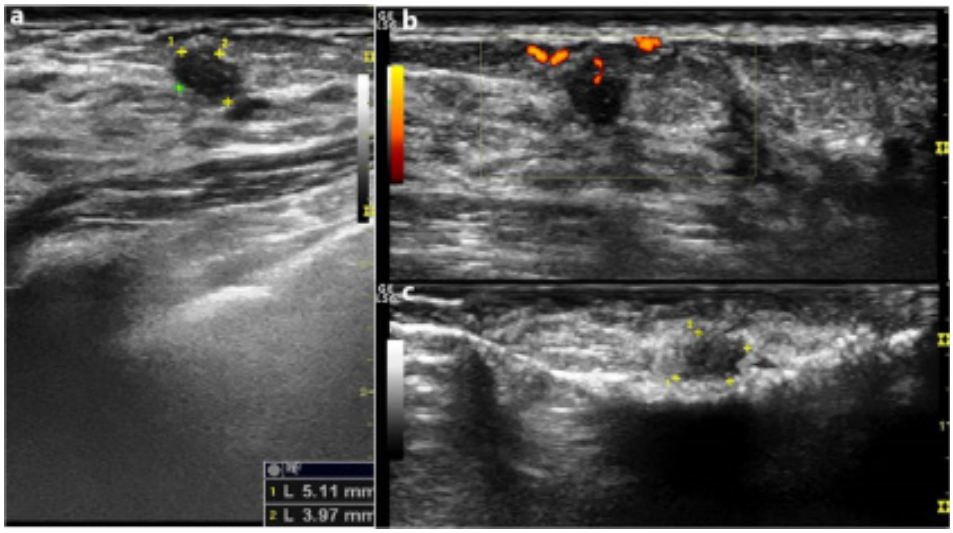

Figure 3. A 42-year-old woman with positive family history a) US image shows a 5 mm hypoechoic mass with angular margins. b) Color doppler shows vascularity within the mass. c) US image of the specimen following stereotaxis. Histopathologic diagnosis was fibrocystic changes.

Statistical analysis

In the evaluation of the findings obtained in the study, statistical analyses were performed using the IBM SPSS Statistics 22 (SPSS IBM, Turkey) software. In the study, measurements were performed as mean, standard deviation, median and frequency in the evaluation of descriptive statistics. Three and multiple groups with non-normal distribution were compared using the Kruskal-Wallis test, and the Chi-square test and Fisher Freeman Halton tests were used for the comparison of categorical data. Significance was evaluated at $p<0.05$.

RESULTS

In the study, 82 breast lesions in 82 women with range between 27 and 69 years (mean 46.87±10.13 years) were evaluated. The lesions were in the right breast in 45 of the patients, and in the left breast in 37 patients. The most common localization was the upper outer quadrant (53.7%). Demographic data of the patients were presented in detail in Table 1.

Histopathologically, the most common benign lesions were fibroadenoma (n=26, 31.7%) and fibrocystic changes (n=15, 18.3%). The proportion of the remaining pathological diagnosis groups was smaller than 10%, and 7 patients (8.5%) were classified as "non-specific" (Table 1).

Table 1. Distribution of demographic parameters

	Mean±SD	**Min-Max**
Age (years)	**46.87±10.13**	**27-69**
		n (%)
Side	Right	45 (54.9%)
	Left	37 (45.1%)
Family history	No	61 (74.4%)
	Yes	21 (25.6%)
Biopsy procedures	US-guided core needle	49 (59.8%)
	US-guided stereotaxis	19 (23.2%)
	US-guided core needle+ stereotaxis	14 (17.1%)
Histopathological diagnoses	Fibroadenoma	26 (31.7%)
	Sclerosing adenosis	7 (8.5%)
	Fibrocystic changes	15 (18. 3%)
	Inflammation-mastitis	5 (6.1%)
	Intraductal papilloma	7 (8.5%)
	Fibrosis	4 (4.9%)
	Atypical ductal hyperplasia	2 (2.4%)
	Fat necrosis	6 (7.3%)
	Radial scar	3 (3.7%)
	Non-specific	7 (8.5%)

In the ultrasonography, margins of the lesions were smooth-macrolobulated in 30%, microlobulated in 12.2%, indistinct-irregular in 39%, angular in 15.9%, and spiculated in 2.4% (Table 2). The majority of smooth-macrolobulated (13/25) and microlobulated (5/10) lesions were diagnosed with "fibroadenoma", the majority of lesions with indistinct-irregular (9/32) margins were diagnosed with "fibrocystic change". Two lesions with spiculated margins were diagnosed as "radial scar". However, no statistically significant difference was found between the pathological diagnosis groups in terms of US findings such as the margins of the lesions, the presence of microcalcifications and posterior shadowing (p1:0.088, p2:1.000 and p3:0.063, respectively) (Table 3). No significant difference was found between the pathological diagnosis groups in terms of patient age, lesion size and presence of suspicious axillary lymph nodes (p1:0.239, p2:0.369 and p3:0.073, respectively).

According to the BI-RADS category, 48 (58.5%) lesions were classified as 4a, 29 (35.4%) lesions were classified as 4b, 3 (3.7%) were classified as 4c, and 2 (2.4%) were classified as 5. The pathological diagnosis of the lesions according to BI-RADS classification was presented in Table 4. In the statistical analysis, the incidence of fibroadenoma was found to be significantly higher in the BI-RADS 4a group compared to the patients in the other pathological diagnosis group (p:0.007).

Table 2. Distribution of sonographic findings

	Min-Max	Mean±SD(medyan)
Sonographic tumor size (mm)	**5-10**	**8.96±1.46 (10)**
		n (%)
Sonographic margin	Smooth-macrolobulated	25 (30.5%)
	Microlobulated	10 (12.2%)
	Indistinct-irregular	32 (39%)
	Angular	13 (15.9%)
	Spiculated	2 (2.4%)
Microcalcification	No	77 (93.9%)
	Yes	5(6.1%)
Acoustic shadowing	No	76 (92.7%)
	Yes	6(7.3%)
Suspicious axillary	No	76 (92.7%)
lymph node	Yes	6 (7.3%)
BI-RADS score	4[a]	48 (58.5%)
	4[b]	29(35.4%)
	4[c]	3 (3.7%)
	5	2 (2.4%)

Table 3. Sonographic findings of lesions according to pathological diagnosis groups

Histopathological diagnoses	Sonographic margin					Microcalcification	Acoustic shadowing
	Circumscribed macrolobulated	Microlobulated	Indistinct irregular	Angular	Spiculated		
Fibroadenoma	13 (50%)	5 (19.2%)	6 (23.1%)	2 (7.7%)	0 (0%)	3 (11.5%)	0 (0%)
Sclerosing adenosis	2 (28.6%)	0 (0%)	3 (42.9%)	2 (28.6%)	0 (0%)	1 (14.3%)	1 (14.3%)
Fibrocystic changes	2 (13.3%)	1 (6.7%)	9 (60%)	3 (20%)	0 (0%)	1 (6.7%)	2 (13.3%)
Inflammation-mastitis	2 (40%)	1 (20%)	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intraductal papilloma	1 (14.3%)	1 (14.3%)	3 (42.9%)	2 (28.6%)	0 (0%)	0 (0%)	1 (14.3%)
Fibrosis	2 (50%)	0 (0%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)	2 (50%)
Atypical ductal hyperplasia	0 (0%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
Fat necrosis	0 (0%)	1 (16.7%)	4 (66.7%)	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Radial scar	0 (0%)	0 (0%)	1 (33.3%)	0 (0%)	2 (66.7%)	0 (0%)	0 (0%)
Non-specific	3 (42.9%)	1 (14.3%)	2 (28.6%)	1 (14.3%)	0 (0%)	0 (0%)	0 (0%)
P*	**0.088**					**1.000**	**0.063**

Data is given as the number (n) and percentage (%) of the patients. *: Fisher Freeman Halton Test p<0.05

Table 4. Distribution of lesions in BI-RADS according to pathological diagnosis groups

Histopathological diagnoses	BI-RADS classification			
	4a	4b	4c	5
Fibroadenoma (26)	20 (76.9%)	6(23.1%)	0 (0%)	0 (0%)
Sclerosing adenosis (7)	2(28.6%)	5(71.4%)	0 (0%)	0 (0%)
Fibrocystic changes (17)	8(53.3%)	6 (40%)	1(6.7%)	0 (0%)
Inflammation-mastitis (5))	3 (60%)	2 (40%)	0 (0%)	0 (0%)
Intraductal papilloma (7)	3 (42.9%)	4 (57.1%)	0 (0%)	0 (0%)
Fibrosis (4)	2 (50%)	2 (50%)	0 (0%)	0 (0%)
Atypical ductal hyperplasia (2)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
Fat necrosis (6)	2 (33.3%)	3 (50%)	1 (6.7%)	0 (0%)
Radial scar (3)	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)
Non-specific (7)	6 (85.7%)	1 (14.3%)	0 (0%)	0 (0%)
Total (82)	48 (58.5%)	29(35.4%)	3 (3.7%)	2 (2.4%)

DISCUSSION

With the increased use of ultrasonography in routine breast imaging, the BI-RADS system recommended by the American College of Radiology (ACR) has been widely used in order to assess the morphology of the lesions and standardize the terminology of reporting. According to BI-RADS-US lexicon, category 3 assessment represents <2% likelihood of malignancy, while category 5 assessment represents ≥95% likelihood of malignancy. Category 4 represents the wide range of 2-94%. For this reason, category 4 is reported by classifying as 4a (2-10%, low risk), 4b (10-50%, moderate risk) and 4c (50-94%, high risk) in our department, as in many centers.

In our study, the most common benign breast lesion was fibroadenoma. Most of our cases were categorized as 4a, and the incidence of 'fibroadenoma' was found to be statistically high in group 4a. Although 50% of fibroadenomas have smooth-macrolobulated margins, we found that indistinct- irregular margins were the most common type. The least common sonographic findings were the spiculated margin, microcalcification, posterior shadowing and the presence of suspicious axillary lymph nodes.

Solid breast lesions can be classified as benign, intermediate and malignant. Spiculated, angular or microlobuled margins, microcalcifications, marked hypoechogenicity, posterior shadowing and vertical growth have been reported to be highly predictive of malignancy (14). Ellipsoid shape, well-defined margins and the presence of macrolobulation are accepted as predictive features for benign lesions (15). Rahbar et al. demonstrated that the most predictive findings for benign lesions were smooth or macrolobulated margins, rounded or ellipsoid shapes with low inter-observer variability and high rates (16).

Elverici et al. reported the mean lesion size as 10.9±5.57 mm among BI-RADS 4 non-palpable breast lesions in their ultrasonography study (11). They found that 22% of benign lesions were well-circumscribed, 25% had indeterminate borders, 47% had microlobulated, and 7% had angular margins. They recommended that these margins should not be considered as significant signs of malignancy in patients with BI-RADS 4 lesions, especially in oval and small lesions, since microlobulated, indistinct and angular margins were difficult to distinguish.

In our study, 39% of benign lesions were found to have indistinct-irregular margins, 15.9% had angular margins, and 12% microlobulated margins, while 30% of them had smooth-macrolobulated margins. Although the rate of having smooth margins is expected to be high in benign lesions, the indistinct, microlobulated and angular margin characteristics were also detected in benign lesions at remarkable rates, as in our study and the study by Elverici. We believe that as the size of the lesion gets smaller, it becomes difficult to differentiate the margins from from each other, the interobserver variability increases and the experience the experience of the radiologist are effective factors in determining the characteristics of the margins.

In another study that was conducted with patients, who were reported as category 4 by ultrasonography, were diagnosed as benign, and had a mean lesion size of 15 mm, the most common diagnoses were fibroadenoma (38%), sclerosing adenosis (18%) and fibrocystic changes (14%) (17). They described the most common features of margins were indistinct and microlobulated in fibroadenomas, irregular-indistinct margins in sclerosing adenosis, and microlobulated margin and posterior shadowing in fibrocystic changes. On the contrary, we found the most common features of margins as smooth-macrolobulated margins in fibroadenomas, and as indistinct-irregular margins in fibrocystic changes. The indistinct-irregular margin was mostly present in the diagnosis group of fibrocystic diseases; however, we did not find a statistically significant difference between the diagnostic groups.

In our study, among the BI-RADS groups with a higher probability of malignancy, there were 3 patients with category 4c and 2 patients with category 5. In the two patients with category 5, the lesions were described as spiculated margin; however, there were no findings of microcalcification and posterior shadowing. Indistinct-irregular margins were observed in 3 patients in category 4c, and posterior shadowing was observed in 1 patient; and none of them had microcalcifications. In these 5 patients, excision was performed following core biopsy due to radiological-pathological discordance. Two patients with pathological diagnoses of category 5 were reported as radial scar, and 3 patients in category 4c were reported as radial scar, fat necrosis and fibrocystic changes. Since imaging findings of radial scar are in the form of spiculated lesions and structural distortions, it is not possible to distinguish it from cancer by imaging. Fat necrosis is a benign lesion with a spectrum of symptoms ranging from a simple fat cyst to a mass lesion with irregular borders, and it cannot be distinguished from cancer when irregularly border. As in our patients, malignancy should be excluded in these lesions with biopsy. In this study, since the spiculated margins were seen in very few benign lesions and the presence rates of microcalcification and posterior shadowing were low, we believe that these findings are more predictive of malignancy, as mentioned in the literature.

This study has several limitations. First of all, the features of the margins, the presence of microcalcification and posterior shadowing were recorded from the reports due to the retrospective design of the study. Normally, the characteristics of the lesions can be evaluated in more detail with real-time US. Second, we were not able to use the findings of shape, orientation, vascularity and elasticity, which were mentioned in the last version of the BI-RADS atlas, since these data were not reported together in all reports. Other limitations are the inability to analyze interobserver and intra-observer variability due to the

retrospective design of our study, and the small number of cases in some subgroups such as BI-RADS 4c-5.

CONCLUSION

In this study, it was concluded that the possibility of fibroadenoma was higher in lesions defined as BI-RADS 4a, and half of these lesions had smooth-macrolobulated margins. Indistinct-irregular, microlobulated and angular margin features can also be observed significantly in benign lesions, and as the size of the lesion gets smaller, it becomes difficult to distinguish the margin features ; therefore they should be evaluated more carefully.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *This study was planned retrospectively, was checked for compliance with the Helsinki Declaration of Human Rights and was approved by the ethics committee of our hospital before the study (22.03.2021-107/14).*

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