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Research Article

Imaging Features and Histopathological Analysis in Patients with Subcentimeter Breast Cancer Detected by Ultrasonography

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Abstract

Objectives: We aimed to present preoperative ultrasonographic features, distribution of histopathological diagnosis and molecular subtypes of malignant tumors, and to compare sonographic and pathological tumor dimensions in patients with subcentimeter breast lesions.

Methods: Eighty six women with newly diagnosed breast cancer were included in the study who underwent preoperative biopsy and surgical resection between 2015 and 2020. Sonographically tumor margins were grouped as circumscribed, microlobulated, irregular-indistinct, angular and spiculated. By taking 25% of the pathological tumor size and value of ± 5 mm as cut-off, the presence of sonopathological concordance was evaluated.

Results: The median tumor sizes were 10 mm (4-10 mm) sonographically and 11 mm (2-45 mm) histopathologically. The spiculated and irregular-indistinct margins were the most frequent sonog-raphic features (35% and 35%). Value of ±5 mm and 25% of the pathological tumor size acording to cut-off, the sonopathological concordance rates were calculated as 74% and 55%, the underestimation rates were 20% and 35%, the overestimation rates were 6% and 10%, respectively.

Conclusion: In our study, the most common sonographic features was spiculated and irregular-indistinct margins. We found sonopathological concordance rates similar to current literature. Especially in patients with DCIS, invasive lobular carcinoma, and HER2 enriched subtype, sonopathological discordance should be considered when planning the optimal treatment.

Keywords: Breast cancer, concordance, ultrasonography, tumor size, subcentimeter

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Primary tumor size and nodal status are the most important basic parameters for predicting prognosis and planning clinical management in breast cancer patients.[1–3] With technological advances in imaging and screening programs, an increasingly significant portion of newly diagnosed breast cancer cases are women with tumors 1 cm or smaller. As a result, survival rates have increased significantly with early diagnosis and multidisciplinary treatment approaches.[4,5]

Optimal screening for breast cancer detection occurs when the lesion is small and unifocal and when there is no evidence of lymph node involvement and metastasis.[1,3] In the detection of breast cancer today, ultrasonography (US) is the most important highly sensitive additional modality to

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complement mammography. This is because it is easily accessible, repeatable, free of ionizing radiation, and capable of differentiating cystic and solid lesions.[6] The margins of the lesion are the most important sonographic feature when evaluating the character of the breast lesion. Microlobulated, angular, or spiculated margins; the presence of microcalcification; prominent hypoechogenicity; and posterior shadowing are signs in favor of malignancy, while the ellipsoid shape, macrolobulation, and smooth margins indicate a benign lesion.[7]

There are very few studies in the literature that focus on imaging in subcentimeter breast tumors in different modalities.[8–10] However, to our knowledge, there is no US study in the literature reporting the relationship between tumor margin features and molecular subtyping or pathological results in patients with breast tumors ≤10 mm. This study aimed to present preoperative ultrasonographic features, the distribution of histopathological diagnosis, and molecular subtypes of malignant tumors and to compare sonographic and pathological tumor dimensions with two different cutoff values in patients with subcentimeter breast cancer.

Methods

Patient Population

The local Ethics Committee approved this retrospective study with a protocol number of 2020-07-01/288, and informed consent was waived. Eighty-six female patients were included in the study. Each of them was admitted between 2015 and 2020 with a solid mass of 10 mm or smaller with suspected malignancy in breast US and underwent preoperative biopsy procedures and surgical resection at our hospital (Fig. 1). Patients with multifocal and/or multicentric malignancies who received neoadjuvant chemotherapy were excluded from the study. The diagnosis of malignancy in all cases was confirmed histopathologically after surgical excision, breast-conserving surgery, or mastectomy.

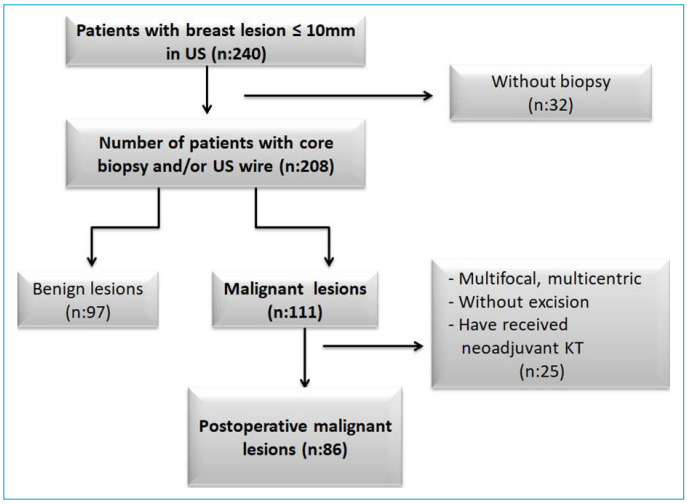

Figure 1. Flow chart showing criteria of inclusion in patients with subcentimeter breast lesions.

Imaging and Interpretation

Breast US was performed with 5–12 MHz linear probe (Affiniti 70 US system, Philips Healthcare, Bothell, WA, USA) by an experienced breast radiologist. Lesions were classified using the Breast Imaging Reporting and Data System (BI-RADS) and the US findings.[11] Tumor margins were grouped sonographically as (1) circumscribed, (2) microlobulated, (3) irregular-indistinct, (4) angular, and (5) spiculated (Figs. 2 and 3). The longest dimension of the lesions was measured in millimeters by excluding the hyperechoic halo around it and compared by taking the tumor size determined by

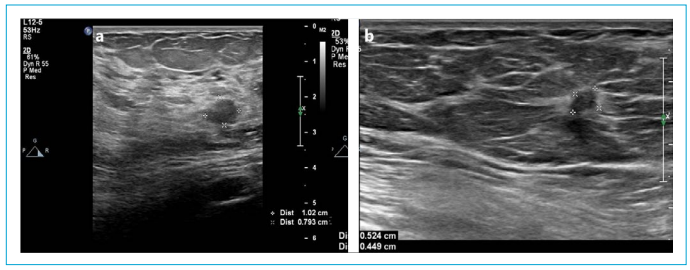

Figure 2. (a) A 48-year-old woman with luminal A molecular subtype, invasive carcinoma. US image shows microlobulated margins hypoechoic mass. The longest dimension of the mass was 10 mm, and the pathologic size was also 11 mm. Sonopathological concordance was in the tumor. **(b)** A 63-year-old woman with luminal A molecular subtype, invasive carcinoma. US image shows indistinct-irregular margins hypoechoic mass. The longest sonographic dimension of the mass was 5 mm, and the pathological dimension was 6 mm. Sonopathological concordance was in the tumor.

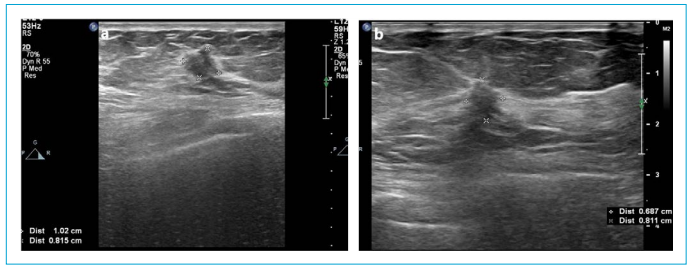

Figure 3. (a) A 61-year-old woman with luminal A molecular subtype, invasive carcinoma. US image shows angular margins hypoechoic mass. The longest sonographic dimension of the mass was 10 mm, and the pathologic size was 9 mm. Sonopathological concordance was in the tumor. **(b)** A 62-year-old woman with luminal B HER2 (-) molecular subtype, invasive carcinoma. US image shows spiculated margins hypoechoic mass. The longest sonographic dimension of the mass was 8 mm, and the pathologic size was 8 mm. Sonopathological concordance was in the tumor.

pathology examination as a reference. A cutoff value of ± 5 mm was used when comparing histopathological and sonographic dimensions. If there was a difference of 5 mm or less between sonographic and pathological dimensions, it was considered sonopathological concordance. If there was a difference of more than 5 mm, it was considered sonopathological discordance (underestimation/overestimation).[12,13] By using 25% of the pathological tumor size as a cutoff, the presence of sonopathological concordance was also evaluated.[14]

Histopathological Analysis

Malignant tumors were classified according to histological grades and grouped into three grades (Table 1). They were grouped according to histological type as ductal carcinoma in-situ (DCIS), lobular carcinoma in-situ (LCIS), invasive carcinoma (nonspecific type, NST), invasive lobular carcinoma, and other (tubular, papillary, medullary, mixed, micropapillary, and apocrine carcinoma). The largest tumor size, the involvement of metastatic lymph nodes, and lymphovascular invasion were recorded. Invasive breast carcinomas were divided into five molecular subtypes according to estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor 2 (HER2) receptors on the cell surface, and the Ki-67 proliferation index (Table 1).[15]

Statistical Analysis

The study data, including the suitability of the parameters to the normal distribution, was evaluated using the Shapiro Wilks test. The one-way ANOVA test was used for intergroup comparisons of normally distributed parameters in comparison with quantitative data, and Tamhane's T2 test was used to determine the group that caused the difference. The Kruskal Wallis test was used for intergroup comparisons of parameters that did not show a normal distribution, and Dunn's test was used to determine the group that caused the difference. The chi-square test and Fisher Freeman Halton test were used to compare qualitative data. Significance was evaluated at the $p<0.05$ level.

Results

Lesion Characteristics According to Sonographic, Histologic, and Molecular Subgroups

The age of the patients in the study ranged from 23 to 73 years (mean = 53.94±10.26 years). The demographic data and sonographic findings of the patients are given in detail in Table 1.

The most common histopathological diagnosis was invasive carcinoma (NST), with a rate of 69% (Table 1). When compared in terms of US margin features according to

Table 1. Distribution of demographic parameters

	Min-Max	Mean±SD
Age (years)	23-73	53.94±10.26
Sonographic tumor size (mm)(n=86) (median)	4-10	8.84±1.48 (10)
Pathology tumor size (mm)(n=82) (median)	2-45	12.26±6.29 (11)
	n	**%**
Side		
Right	42	48.8
Left	44	51.2
Localization		
Upper outer quadrant	48	55.8
Upper inner quadrant	17	19.8
Lower outer quadrant	9	10.5
Lower inner quadrant	8	9.3
Retroareolar	4	4.7
Family history		
No	66	76.7
Yes	20	23.3
US margin		
Circumscribed	2	2.3
Microlobulated	9	10.5
Indistinct-irregular	30	34.9
Angular	15	17.4
Spiculated	30	34.9
Microcalcification		
No	70	81.4
Yes	16	18.6
BI-RADS score		
4a	7	8.1
4b	23	26.7
4c	26	30.2
5	30	34.9
Pathological type		
DCIS	9	10.5
LCIS	1	1.2
Invasive carcinoma (NST)	59	68.6
Invasive lobular carcinoma	7	8.1
Other*	10	11.6
Histologic grade		
1	29	33.7
2	37	43
3	20	23.3
Molecular subtypes (n=76)		
Luminal A	47	61.8
Luminal B (HER2 -)	17	22.4
Luminal B (HER2 +)	8	10.5
HER2 enriched	4	5.3
Triple-negative	0	0
Axillary lymph node metastasis (n=76)		
No	62	81.6
Yes	14	18.4
Lymphatic vessel invasion (n=76)		
No	64	84.2
Yes	12	15.8

* Other malignant lesions; It were tubular in 3 cases, papillary in 3, mixed in 1, medullary in 1, micropapillary in 1 and apocrine carcinoma in 1. DCIS: ductal carcinoma in situ, LCIS: lobular carcinoma in situ.

histological diagnoses, a statistically significant difference was found between them (p=0.003). The spiculated margin rates were found to be statistically significantly lower in patients with DCIS compared to invasive carcinoma (NST), invasive lobular carcinoma and other groups (p1=0.003; p2=0.009; p3=0.008). The irregular-indistinct margin rates were found to be statistically significantly higher in patients with invasive carcinoma (NST) than the cases in the other group (p=0.016). There is no statistically significant difference between histopathological diagnoses in terms of sonographic size, presence of microcalcification, and distribution rates of BI-RADS (respectively $p_1 = 0.812$, $p_2 = 0.476$, p3 = 0.275).

Molecular subtype was not specified in the pathology report of ten patients with in-situ carcinoma. For 76 invasive breast cancer patients, the sonographic and pathological characteristics of the molecular subtypes are given in Table 2. The mean age of the group with in-situ carcinoma was

Table 2. The relationship between molecular subtypes and study parameters

	Molecular subtypes					p
	DCIS+LCIS Mean±SD	**Luminal A Mean±SD**	**Luminal B (HER2 -) Mean±SD**	**Luminal B (HER2 +) Mean±SD**	**HER2 enriched Mean±SD**	
Age (years)	47.4±5.25	55.28±8.92	53±13.15	59.75±8.28	47±16.39	[1]0.048*
Sonographic tumor size (mm) (median)	9.1±1.29 (9.5)	8.49±1.7 (9)	9.15±1.03 (10)	9.44±1.05 (10)	9.75±0.5 (10)	[2]0.262
Pathology tumor size (mm) (median)	6.5±5.24(4)	11.47±6.23(10)	14.41±6.05(13)	14.13±5.57 (12.5)	17.25±3.86(15.5)	[2]0.004*
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Sonographic margin						
Circumscribed	0 (0)	1 (2.1)	1 (5.9)	0 (0)	0 (0)	[3]0.337
Microlobulated	1 (10)	5 (10.6)	1 (5.9)	1 (12.5)	1 (25)	
Indistinct-irregular	8 (80)	14 (29.8)	4 (23.5)	3 (37.5)	1 (25)	
Angular	0 (0)	10 (21.3)	5 (29.4)	0 (0)	0 (0)	
Spiculated	1 (10)	17 (36.2)	6 (35.3)	4 (50)	2 (50)	
Microcalcification						
No	7 (70)	38 (80.9)	16 (94.1)	7 (87.5)	2 (50)	[4]0.191
Yes	3 (30)	9 (19.1)	1 (5.9)	1 (12.5)	2 (50)	
BI-RADS score						
4a	2 (20)	3 (6.4)	2 (11.8)	0 (0)	0 (0)	[3]0.475
4b	5 (50)	11 (23.4)	5 (29.4)	2 (25)	0 (0)	
4c	2 (20)	17 (36.2)	3 (17.6)	2 (25)	2 (50)	
5	1 (10)	16 (34)	7 (41.2)	4 (50)	2 (50)	
Diagnosis						
Invasive carcinoma (NST)		36 (76.6)	13 (76.5)	7 (87.5)	3 (75)	[3]0.437
Invasive lobular carcinoma		6 (12.8)	0 (0)	1 (12.5)	0 (0)	
Other		5 (10.6)	4 (23.5)	0 (0)	1 (25)	
Histologic grade						
1	2 (20)	26 (55.3)	1 (5.9)	0 (0)	0 (0)	[3]0.000*
2	4 (40)	14 (29.8)	12 (70.6)	6 (75)	1 (25)	
3	4 (40)	7 (14.9)	4 (23.5)	2 (25)	3 (75)	
Lymphatic vessel invasion						
No	-	39 (83)	15 (88.2)	6 (75)	4 (100)	[4]0.809
Yes	-	8 (17)	2 (11.8)	2 (25)	0 (0)	
Axillary lymph node metastasis						
No	-	37 (78.7)	14 (82.4)	7 (87.5)	4 (100)	[4]0.957
Yes	-	10 (21.3)	3 (17.6)	1 (12.5)	0 (0)	

[1]Oneway Anova Test; [2]Kruskal Wallis Test; [3]Ki-Kare Test4Fisher Freeman Halton Test; *p<0.05; DCIS: ductal carcinoma in situ, LCIS: lobular carcinoma in situ, Data are given as n (%).

found to be statistically significantly lower than the luminal A and luminal B HER2+ groups ($p_1 = 0.012$, $p_2 = 0.035$). There was no statistically significant difference between the other molecular subtype groups in terms of mean age (p3 = 0.761; p4 = 1.000). Histopathological tumor size in the in-situ carcinoma group was found to be statistically significantly lower than luminal B HER2-, luminal B HER2+, and HER2 enriched groups ($p_1 = 0.006$, $p_2 = 0.011$, $p_3 = 0.001$). Histopathological tumor size in the Luminal A group was found to be statistically significantly lower than the HER2 enriched group (p=0.014). The rate of histological grade 1 in the luminal A group was 55%; it was statistically significantly higher thanluminal B HER2-, luminal B HER2+, and HER2 enriched groups ($p_1 = 0.002$; p2 = 0.005; p3 = 0.014). There is no statistically significant difference between the other molecular subtype groups in terms of tumor grade distribution rates.

Accuracy in Tumor Size Measurements

Sonographically, tumor sizes range from 4 to 10 mm, with a median of 10 mm. Histopathologically, tumor sizes range from 2 to 45 mm, with a median of 11 mm. Histopathological tumor size was not reported for the four patients with a diagnosis of DCIS. While comparing histopathological and sonographic dimensions in the other 82 patients, a cutoff value of ± 5 mm was used, and the sonopathological concordance rate was calculated as 74%, the underestimation rate as 20%, and the overestimation rate as 6%. When 25% of the pathological tumor size was used as the cutoff value, the concordance rate was calculated as 55%, the underestimation rate as 35%, and the overestimation rate as 10%.

In comparison, by using a ± 5 mm cutoff value between histopathological diagnosis groups, the sonopathological concordance rate in the group with DCIS was found to be statistically significantly lower than the other three diagnostic groups ($p_1 < 0.001$, $p_2 = 0.030$, $p_3 = 0.007$). The sonopathological concordance rate in the invasive carcinoma (NST) group (85%) was statistically significantly higher than the invasive lobular carcinoma group (43%) (p=0.024). When 25% of the tumor size was used as the cutoff value, only the concordance rate of the DCIS group was significantly lower than the invasive carcinoma and other groups ($p_1<0.001$, $p_2 = 0.023$). There is no statistically significant difference between the other groups (Table 3).

There is no statistically significant difference between molecular subtype groups with a cutoff value of ± 5 mm

Table 3. The relationship between sonopathological compatibility and study parameters

	Cut-off 5 mm			p	Cut-off tm size %25			p
	Underestimate n (%)	Concordance n (%)	Overestimate n (%)		Underestimate n (%)	Concordance n (%)	Overestimate n (%)	
Diagnosis								
DCIS	0 (0%)	1 (20%)	4 (80%)	0.000*	1 (20%)	0 (0%)	4 (80%)	0.000*
Invasive carcinoma (NST)	8 (13.6%)	50 (84.7%)	1 (1.7%)		19 (32.2%)	38 (64.4%)	2 (3.4%)	
Invasive lobular carcinoma	4 (57.1%)	3 (42.9%)	0 (0%)		4 (57.1%)	2 (28.6%)	1 (14.3%)	
Other	4 (40%)	6 (60%)	0 (0%)		5 (50%)	4 (40%)	1 (10%)	
Molecular subtypes								
Luminal A	8 (17)	38 (80.9%)	1 (2.1%)	0.666	14 (29.8%)	29 (61.7%)	4 (8.5%)	0.125
Luminal B (HER2 -)	5 (29.4%)	12 (70.6%)	0 (0%)		7 (41.2%)	10 (58.8%)	0 (0%)	
Luminal B (HER2 +)	1 (12.5%)	7 (87.5%)	0 (0%)		3 (37.5%)	5 (62.5%)	0 (0%)	
HER2 rich	2 (50%)	2 (50%)	0 (0%)		4 (100%)	0 (0%)	0 (0%)	
Histologic grade								
Grade 1	3 (10.3%)	24 (82.8%)	2 (6.9%)	0.403	5 (17.2%)	20 (69%)	4 (13.8%)	0.055
Grade 2	8 (22.2%)	25 (69.4%)	3 (8.3%)		14 (38.9%)	18 (50%)	4 (11.1%)	
Grade 3	5 (29.4%)	12 (70.6%)	0 (0%)		10 (58.8%)	7 (41.2%)	0 (0%)	
Sonographic margin								
Microlobulated	2 (22.2%)	6 (66.7%)	1 (11.1%)	0.622	3 (33.3%)	3 (33.3%)	3 (33.3%)	0.123
Indistinct-irregular	6 (23.1%)	17 (65.4%)	3 (11.5%)		11 (42.3%)	12 (46.2%)	3 (11.5%)	
Angular	2 (13.3%)	12 (80%)	1 (6.7%)		3 (20%)	11 (73.3%)	1 (6.7%)	
Spiculated	6 (20%)	24 (80%)	0 (0%)		12 (40%)	17 (56.7%)	1 (3.3%)	

Ki-Kare Test; *p < 0.05; Note1: Lobular carcinoma in situ diagnosis was excluded from the analysis since n = 1; Note2: Those with circumscribed Sonographic margin are excluded from the analysis since n = 2; DCIS: ductal carcinoma in situ, *Other malignant tumorss were medullary, tubular, papillary, micropapillary, and apocrine carcinoma.

in terms of sonopathological concordance (p=0.666). The sonopathological concordance rate in the HER2 enriched group with a 25% cutoff value was found to be statistically significantly lower than the luminal A group (p=0.026). There is no statistically significant difference between the other molecular subtype groups in terms of sonopathological concordance with this cutoff value (Table 3).

Discussion

Traditionally, malignant breast masses are expected to show poorly demarcated or spiculated margins. However, there are studies showing that well-demarcated margins are more likely to represent higher-grade tumors.[16] Therefore, the relationship between tumor grade and US findings is variable. Blaichman et al. evaluated 299 invasive ductal carcinomas with a mean tumor size of 15 mm and defined sonographic findings according to histological grade.[17] Although the distribution of spiculated and angular types is similar across histological grades, they found that grade 3 lesions have more microlobules and less indistinct margins and that the indistinct margin trait, which is a good indicator of malignancy, is not a good predictor of histological grade. In this study, we found that the most frequent sonographic features are the spiculated and irregular-indistinct margins. Circumscribed margins were only present in two cases, and these cases were diagnosed as invasive papillary carcinoma. We found no significant relationship between histological grade and US margin features. We believe that if lesions of 10 mm or less are circumscribed and do not grow in size during follow-up, they will be considered benign, and the likelihood of malignancy will be difficult to predict. However, even if the lesion is circumscribed, the internal nature of the lesion should be examined more carefully with high-resolution instruments.

It is known that 75% of breast tumors have estrogen and/or progesterone receptors, meaning that most tumors are in the luminal group. HER2 enriched tumors are found in 15–25% of invasive breast cancers and show a worse prognosis but respond well to HER2-targeted therapies.[18] In a retrospective study with breast cancers smaller than 10 mm postoperatively, 75% of patients were in the ER/PR+ and HER2- group, 13% were in the HER2+ group, and 11% were in the triple-negative group.[19] These findings are consistent with other studies done independent of tumor size. Our luminal tumor rates were higher than the literature, and our HER2 enriched rate was low. These results may be related to the small sample size and the low number of cases in the nonluminal group.

Au et al. reported that spiculated margins were more common in ER and PR positive tumors and that microlobule margins were more common in ER and PR negative tumors; no difference was found between HER2+ and HER2- tumors.[20] It was reported in another study that luminal A, B, and HER2 tumors were more closely related to indistinct and spiculated margins and that they were less closely related with angular and microlobule margins.[21] Unlike these studies, we did not find a significant relationship between molecular subtypes and lesion margin features in this patient group.

The triple-negative subtype constitutes 15%–20% of breast cancers, has the poorest prognosis of all subtypes, has high proliferation rates, and are mostly high-grade tumors. They tend to show a combination of circumscribed margins and posterior acoustic enhancement in US and can sometimes be misinterpreted as benign.[22] Interestingly, there were no triple-negative cases in our study. These results may be associated with the relatively small patient population in our study, the small size of the tumors, the fact that triple-negative tumors may have been evaluated as benign sonographically and the fact that we may not have been able to detect these lesions with high proliferation rates within the scanning periods since they are smaller than 10 mm.

Accurate information about the size of the mass is required to boost the patient's cosmetic satisfaction by minimizing the loss of normal breast tissue and the full excision of the breast tumor.[23] Preoperative tumor size measurement is performed by multimodal imaging methods. However, postoperative histopathological measurement of tumor size is considered the gold standard. The compatibility between the estimated tumor size determined by imaging studies and the actual tumor size determined by pathological examination is used to test the imaging modality's efficiency and accuracy. Studies have been conducted using different cutoff values for compatibility, but today, a ± 0.5 cm cutoff value is the most widely accepted threshold.[12,13]

There are studies showing that sonographic tumor size measurement is highly compatible with pathological findings.[12,14,23] Xu et al. used a cutoff value of ± 0.5 cm, and they reported a sonopathological concordance rate of 56% and an underestimation rate of 27%.[13] They stated that the underestimation rate is higher in high-grade tumors and in HER2+ that the high grade may cause irregular shapes and blurry echoes, and that this may negatively affect the measurement of tumor size. In a study conducted by Lai et al. with different cutoff values, they found that the US concordance rate was higher in T1 stage tumors than MRI (59% and 21%, respectively).[14] They reported that as the T stage increased, the concordance rate of sonography decreased, and the MRI concordance rate increased. Also, they reported that the US is superior to MRI in estimating tumor

size in luminal A, luminal B1, triple-negative, and HER2 enriched subtypes. They found high underestimation rates sonographically in histological subtypes of DCIS, invasive ductal carcinoma+DCIS, and invasive lobular carcinoma. As a result, they said that US should remain the standard in estimating tumor size. In this current study, we found concordance rates with both cutoff values similar to these studies and even higher.

Our study has limitations such as retrospective concept and the exclusion of some sonographic features, such as shape, orientation, vascularity, and elasticity, which were mentioned in the last version of the BI-RADS atlas. Moreover, statistical analysis could not be performed in comparisons of special types of invasive cancers due to the limited number of cases.

Conclusion

In conclusion, in our study, similar to studies conducted regardless of tumor size, the most common sonographic features were spiculated and irregular-indistinct margins, the most common histopathological type was invasive carcinoma (NST), and the most common molecular subtype was luminal A in patients with subcentimeter malignant breast tumors. We found sonopathological concordance rates similar to the current literature. But especially in patients with DCIS, invasive lobular carcinoma, and HER2 enriched subtype, sonopathological discordance should be considered when planning the optimal treatment. Despite the discordance, most of the tumors conform to the T1 stage, and it has been found that 80% of the DCIS cases are overestimated. In addition, the cutoff value of ± 0.5 cm for subcentimeter tumors is a wide range, and using a 25% cutoff value is a more objective method.

Disclosures

Ethics Committee Approval: Hitit University Clinical Research Ethics Committee approved this retrospective study with a protocol number of 2020-07-01/288 and the informed consent was waived.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – N.F., C.Y.; Design – N.F., C.Y.; Supervision – C.Y.; Materials – N.F., C.Y.; Data collection &/or processing – N.F., Z.B.A.,U.H., B.B.; Analysis and/or interpretation – N.F.; Literature search – N.F.; Writing – N.F.; Critical review – C.Y., B.B.

References

1. Elkin EB, Hudis C, Begg CB, Schrag D. The effect of changes in tumor size on breast car-cinoma survival in the U.S.: 1975–1999. Cancer 2005;104:1149–57. [CrossRef]
2. Mirza AN, Mirza NQ, Vlastos G, Singletary SE. Prognostic factors in node-negative breast cancer: a review of studies with sample size more than 200 and follow-up more than 5 years. Ann Surg 2002;235:10–26. [CrossRef]
3. Narod SA, Iqbal J, Jakubowska A, Huzarski T, Sun P, Cybulski C, et al. Are two-centimeter breast cancers large or small? Curr Oncol 2013;20:205–11. [CrossRef]
4. Derici H, Tansug T, Nazlı O, Bozdag AD, Koc O, Varer M, et al. Stereotactic wire localiza-tion and surgical excision of nonpalpabl breast lesions. Eur J Breast Health 2007;3:10–3.
5. Shea B, Boyan WP Jr, Kamrani K, Lepis G, Dupree D, Chang S, et al. Let us cut to the core: is core biopsy enough for subcentimeter breast cancer? J Surg Res 2017;216:30–4. [CrossRef]
6. Nothacker M, Duda V, Hahn M, Warm M, Degenhardt F, Madjar H, et al. Early detection of breast cancer: benefits and risk of supplemental breast ultrasound in asymptomatic women with mammographically dense breast tissue. A systematic review. BMC Cancer 2009;9:335. [CrossRef]
7. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nod-ules: use of sonography to distinguish between benign and malignant lesions. Radiology 1995;196:123–34. [CrossRef]
8. Onishi N, Sadinski M, Gibbs P, Gallagher KM, Hughes MC, Ko ES, et al. Differentiation between subcentimeter carcinomas and benign lesions using kinetic parameters derived from ultrafast dynamic contrast-enhanced breast MRI. Eur Radiol 2020;30:756–66. [CrossRef]
9. Meissnitzer M, Dershaw DD, Feigin K, Bernard-Davila B, Barra F, Morris EA. MRI ap-pearance of invasive subcentimetre breast carcinoma: benign characteristics are com-mon. Br J Radiol 2017;90:20170102. [CrossRef]
10. Xiang LH, Yao MH, Xu G, Pu H, Liu H, Fang Y, et al. Diagnostic value of contrast-enhanced ultrasound and shear-wave elastography for breast lesions of sub-centimeter. Clin Hemorheol Microcirc 2017;67:69–80. [CrossRef]
11. American College of Radiology. BI-RADS: ultrasound, 2nd ed. Breast imaging reporting and data system atlas. 5th ed. Reston, VA: American College of Radiology; 2013.
12. Luparia A, Mariscotti G, Durando M, Ciatto S, Bosco D, Campanino PP, et al. Accuracy of tumor size assessment in the preoperative staging of breast cancer: comparison of digi-tal mammography, tomosynthesis, ultrasound and MRI. Radiol Med 2013;118:1119–36. [CrossRef]
13. Xu J, Ma G, Liang M, Wang Y, Pan H, Li L, et al. Factors that influence ultrasound evalu-ation of breast tumor size. Med Ultrason 2013;21:144–51. [CrossRef]
14. Lai HW, Chen DR, Wu YC, Chen CJ, Lee CW, Kuo SJ, et al. Comparison of the diagnostic accuracy of magnetic resonance imaging with sonography in the prediction of breast cancer tumor size: a concordance analysis with histopathologically determined tumor size. Ann Surg Oncol 2015;22:3816–23.
15. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thürlimann B,

Senn HJ, et al. Strategies for subtypes-dealing with the diversity of breast cancer: highlights of the St Gallen In-ternational Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol 2011;22:1736–47. [CrossRef]
16. Lamb PM, Perry NM, Vinnicombe SJ, Wells CA. Correlation between ultrasound charac-terisitcs, mammographic findings and histological grade in patients with invasive ductal carcinoma of the breast. Clin Radiol 2020;55:40–4. [CrossRef]
17. Blaichman J, Marcus JC, Alsaadi T, El-Khoury M, Meterissian S, Mesurolle B. Sonograph-ic appearance of invasive ductal carcinoma of the breast according to histologic grade. Am J Roentgenol 2012;199:402–8. [CrossRef]
18. Wolff AC, Hammond MEH, Allison KH, Harvey BE, Mangu PB, Bartlett JMS, et al. Hu-man epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol 2018;36:2105–22. [CrossRef]
19. Colonna SV, Higgins AK, Alvarez J, Saville BR, Lawrence J, Abramson VG. Analysis of risk of recurrence by subtype in ≤ 1-cm breast tumors. Clin Breast Cancer 2016;16:223–31.
20. Au FW, Ghai S, Lu FI, Moshonov H, Crystal P. Histological grade and immunohistochem-ical biomarkers of breast cancer: correlation to ultrasound features. J Ultrasound Med 2017;36:1883–94. [CrossRef]
21. Wu T, Li J, Wang D, Leng X, Zhang L, Li Z, et al. Identification of a correlation between the sonographic appearance and molecular subatype of invasive breast cancer: A review of 311 cases. Clin Imaging 2019;53:179–85. [CrossRef]
22. Costantini M, Belli P, Bufi E, Asunis AM, Ferra E, Bitti GT. Association between so-nographic appearances of breast cancers and their histopathologic features and bi-omarkers. J Clin Ultrasound 2016;44:26–33.
23. Ko KH, Jung HK, Park AY, Koh JE, Jang H, Kim Y. Accuracy of tumor size measurement on shear wave elastography (SWE): Correlation with histopathologic factors of invasive breast cancer. Medicine (Baltimore) 2020;99:e23023.