hormone receptor status, lymphovascular invasion, her-2/neu status, p53 expression, histologic grade necrosis, and microcalcifications.

Results: 63 patients (47.4%) were found as solitary lesions. 30 patients (22.6%) were found at another suspicious lesions, NME were found at 40 patients (30.1%). NMEs have been found at younger patients (group 1: 53.7; group 2: 51.6; group 3: 46.1, p = 0.02), tumor sizes and specimen's sizes were not different among three groups, excistence of EIC, necrosis, calcification, lymph vascular invasion, hormone receptor status, histologic grade, her-2/neu status, lymph node status and p53 expressions were not correlated with NME. Histolgic features, such as ductal carcinoma with cribriform type and lobular carcinoma were more found at NME than other groups (p = 0.012) (Table 1). Group 2 were more taken mastectomy than other groups (p = 0.048)(Table 1). In breast conserving operations, the sizes of specimen were not different among three groups, but re-excision rates in NME were higher than other groups (group 1: 1.8%, group 2:9.5%, group: 20%).

Conclusions: NME has not been determined about an exact entity and the clinical significance. It was a small retrospective study, but it needs to get wider excision margins than non-NME contained breast cancers.

	Group 1	Group 2	Group 3	P-value
Age	53.6(±8.7)	51.6(±8.8)	46.1(±7.5)	**<0.001**
Tumor size	2.12(±1.3)	1.6(±1.1)	2.0(±2.0)	0.368
Specimen size	10.8(±3.4)	13.6(±4.8)	12.5(±5.6)	**0.021**
Specimen sized (BCS)	10.0(±2.2)	10.6(±1.7)	10.3(±3.4)	0.637
LN(−)	48	22	31	0.654
LN(+)	15	9	9	
ER(−)	29	12	19	0.806
ER(+)	34	18	21	
PR(−)	38	19	21	0.617
PR(+)	25	11	19	
Histology				**0.012**
DCIS/LCIS	5	4	13	
IDC	18	12	9	
ILC	0	1	0	
Others	3	0	0	
EIC(−)	53	22	28	0.21
EIC(+)	9	8	10	
LVI(−)	53	24	32	0.709
LVI(+)	9	6	8	
Necrosis(−)	35	21	24	0.458
Necrosis(+)	27	9	16	
Microcalcification(−)	40	24	17	0.752
Microcalcification(+)	22	16	13	
Operation				**0.049**
BCS	55	21	30	
MRM	8	9	10	
HG				0.499
low	24	13	12	
high	39	17	28	
p53(−)	42	24	25	0.272
p53(+)	21	6	15	
Her−2/neu(−)	49	22	25	0.244
Her−2/neu(+)	14	9	15	

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Role of Big Endothelin-1 in the Early Diagnosis of Lobular Neoplasia of the Breast

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Background: The endothelins and their receptors, collectively known as the endothelin system, exert important vasoactive properties while they are involved in various cellular processes including tissue differentiation, development, cell proliferation and hormone production. This network is often deregulated in human malignancy, contributing to mitogenesis, angiogenesis, invasion and metastasis, antiapoptosis and immune modulation. The tissue expression of endothelin-1 (ET-1) has been shown to increase during the progression of breast cancer, correlating with the acquisition of malignant potential. As far as its biological precursor Big ET-1 is concerned, clinical data suggest that it is a sensitive indicator of ET-1 activation. The aim of the present study is to investigate plasma ET-1 and Big ET-1 expression in patients with lobular neoplasia of the breast and their potential role in early diagnosis.

Materials and Methods: Peripheral blood samples were collected upon diagnostic biopsy of women with suspicious mammographic abnormalities BI-RADS ⩾4. Among them, 30 patients were diagnosed with lobular neoplasia (Mean age: 52.52±9.22 years) and 32 patients with benign breast lesions (Mean age: 55.68±11.32 years). Plasma ET-1 and Big ET-1 levels were quantitatively determined by enzyme-linked immunosorbent assay.

Results: Significantly higher plasma Big ET-1 levels were observed in patients with lobular neoplasia, compared to those with benign disease (0.72 and 0.33 fmol/ml, respectively, p < 0.0001). On the contrary, plasma ET-1 levels did not differ between the two patient groups (0.81 and 0.82 fmol/ml, respectively).

Table1: ET-1 and its biological precursor, Big ET-1, median plasma levels in patients with lobular neoplasia and benign lesions of the breast

	Lobular Neoplasia (N = 30)	Benign Disease (N = 32)	*p-value*
ET-1 (fmol/ml)	0.81	0.82	NS
Big ET-1 (fmol/ml)	0.72	0.33	<0.0001

Conclusions: Lobular neoplasia (LN) encompasses the entire spectrum of atypical epithelial proliferations in the terminal duct-lobular unit, including atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). LN is regarded as a risk factor for the subsequent development of invasive ductal or lobular carcinoma. To date, scarce data have been reported regarding circulating ET-1 and Big ET-1 levels in breast cancer while there are no studies specifically focusing on lobular neoplasia. This is an original observation of significantly higher plasma levels of Big ET-1 in patients with lobular neoplasia compared to benign breast disease, suggesting that Big ET-1 circulating expression may provide a promising biomarker for the early diagnosis of lobular neoplasia of the breast.

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Sonographic Features of BI-RADS(TM)-US 4 Breast Masses in Luminal, HER2 Overexpression and Triple Negative Phenotypes

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Background: The molecular dissimilarities between breast cancer types often lead to different clinical presentations and maybe correlate with some ultra sonographic (US) features. The purpose of this study was to assess the sonographic characteristics of BI-RADS®-US 4 breast masses in the Luminal, HER2 *overexpression* and Triple Negative phenotypes.

Methods: We consecutively examined a series of 335 women diagnosed as presenting BI-RADS®-US 4 breast masses between March 2009 and December 2010. All masses were biopsied and histological results were classified as malignant (n = 140, 42%) or benign (n = 195, 58%). Estrogen receptor (ER), progesterone receptor (PR) and Human Epidermal Growth Factor Receptor 2 (Her2) expression were assessed, using immunohistochemistry (IHC). For 8 (6%) cases, only ER and PR were evaluated. Lesions with complete IHC assessment were grouped into three phenotypic subtypes: Luminal (89 cases), Her2 overexpression (27 cases) and Triple Negative (16 cases). We then compared the sonographic features of the malignant lesions according to the phenotypic status of the masses. All calculations were performed with SPSS version 15 (SPSS Inc., Chicago IL). This study was approved by our institutional review board and all participants signed an informed consent form.

Results: The positive predictive values (PPV) for subcategories 4a, 4b and 4c of the 335 BI-RADS®-US 4 masses were 16%, 43% and 85%, respectively. Mucinous carcinomas were significantly associated with BI-RADS®-US 4a and 4b categories (p = 0.01). The Luminal phenotype was positively associated with the following sonographic features: spiculated margin (OR=6.4; 95% CI=1.8 to 23.6), indistinct margin (OR=17.2; 95% CI=1.8 to 23.6), echogenic halo (OR=3.8; 95% CI=1.05 to 13.6). The Luminal phenotype was negatively associated with enhancement (OR=0.3; 95% CI=0.15 to 0.76). Triple Negative phenotype was negatively associated with spiculated margin (OR=0.13; 95% CI=0.02 to 0.8) and shadowing (OR=0.02; 95% CI=0.01 to 0.47). The Her2 phenotype was not associated with any of the sonographic features.

Conclusion: Specific sonographic features may be positively related to the Luminal and Triple Negative phenotypes, but the BI-RADS®-US subcategories 4a, 4b and 4c were not associated with the molecular phenotypes of malignant breast masses.