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Breast cancer imaging features as a predictor of the hormonal receptor status, HER2neu expression and molecular subtype

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Abstract

Background: Determination of the hormonal receptor (HR) status, HER2neu expression, and the molecular subtype has valuable diagnostic, therapeutic, and prognostic implications for breast cancer as breast cancer stratification during the last two decades has become dependent upon the underlying biology. The aim of this study is to assess the correlation between imaging features of breast cancer and the HR status, HER2neu expression, and the molecular subtype. Sixty breast cancer patients underwent breast ultrasound, mammography, and MRI evaluation. Pathological evaluation using immunohistochemistry and FISH was used to detect the HR status, HER2/neu expression, and the molecular subtype. Those findings were then correlated with the radiologic data.

Results: HR-positive tumors were associated with posterior acoustic shadowing (34/44, 77.3%; $p = 0.004$). Hormonal-negative tumors presenting as masses were more likely circumscribed on US and MRI compared to hormonal positive mass tumors (6/14, 42.9% vs 3/36, 7.7%; $p = 0.003$ on US and 6/13, 46.3% vs 3/36, 8.3%; $P = 0.007$ on MRI) and had malignant DCE kinetics with washout curves compared to the hormonal positive group (10/16, 62.5% vs 4/44, 9.1%; $P < 0.001$). HER2neu-positive tumors were significantly associated with calcifications and multifocality on mammography compared to HER2neu-negative group (9/13, 69% vs 12/34, 25.5%; $P = 0.007$) and (7/13, 53% vs 3/47, 6%; $P < 0.001$). TNBC and HER2neu-enriched were associated with washout kinetic curve pattern (57.1% and 66.7%, respectively). TNBCs were associated with circumscribed margins on US and MRI (6/9, 66.7%; $P < 0.001$).

Conclusion: Microcalcifications, margins, posterior acoustic features, and malignant washout kinetics strongly correlate with the hormonal receptor status, HER2neu status, and molecular subtype of breast cancer. These findings may suggest the molecular subtype of breast cancer and further expand the role of imaging.

Keywords: Imaging features, Hormonal receptor, HER2neu expression, Molecular subtype, Mammography, Ultrasonography, MRI

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Background

Breast cancer constitutes a diverse group of diseases, which can be appreciated by its variable imaging features, histologic and molecular classifications, and its correspondingly variable disease course [1]. The traditional classification of breast cancer depends on the clinicopathologic analysis of tumors, defining breast cancer by histopathologic features. The tumor size, lymph node involvement, local invasion, and distant metastases were then used to decide the treatment choices [2].

However, the traditional classifications do not fully demonstrate the diversity of breast cancer. During the last two decades, breast cancer classifications have been reshuffled, from the histopathologic type to the molecular subtype [3]. Each molecular subtype presents different incidence, response to treatment, recurrence, prognosis, preferred metastatic organs, and disease-free survival outcomes [4]. A detailed molecular classification is a requirement for appropriate treatment and management as the latest generations of anticancer agents are based on biological mechanisms. Since 2011, the recommendations for breast cancer systemic therapies depend on the molecular subtype as per the St. Gallen International Expert Consensus Panel [5].

Clinical biomarkers play important roles in diagnosis and prediction of prognosis and may also represent therapeutic targets. Key breast cancer biomarkers include ER, PR, and HER2/neu. The expression of those markers correlates with differences in tumor behavior and patient outcome and the potential response to targeted endocrine therapy or HER2 therapy. The protein expression levels of ER, PR, and HER2 are assessed using immunohistochemistry and, in addition, the ERBB2 gene copy number is also quantified using in situ hybridization [6].

Patients with hormone receptor-positive (HR+) breast cancers will likely receive endocrine therapy, while patients with HER2+ breast cancers will receive trastuzumab or other HER2-targeted therapies [7].

As the name suggests, triple-negative breast cancer (TNBC) encompasses all tumors that are negative for ER, PR, and HER2. The majority of TNBC are high grade and aggressive tumors associated with a poorer outcome than other breast cancer subtypes, despite a good response to chemotherapy [8].

Using extensive profiling at the DNA, microRNA, and protein levels, the Cancer Genome Atlas (TCGA) Network classified breast cancer into four molecular subtypes: “luminal A,” “luminal B,” “HER2-enriched,” and “basal-like” [9]. This classification mainly corresponds to hormone receptor and HER2 status and tumoral proliferation [10]. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression status are usually determined by immunohistochemistry (IHC) or fluorescence in situ

hybridization (FISH). This has important therapeutic and prognostic implications [11].

Methods

Sixty breast cancer female patients referred to either the diagnostic radiology department or the clinical oncology and nuclear medicine department from January 2017 to December 2018 were evaluated using mammography, ultrasonography, and breast MRI. Tissue sampling was performed via either image-guided biopsy or surgical excision followed by histopathological examination, IHC for ER, PR, HER2, Ki-67 status assessment and FISH for HER2 equivocal cases.

- Inclusion criteria are as follows:
 - female gender, age more than 18 years old, and pathological diagnosis of invasive breast carcinoma.
- Exclusion criteria are as follows:
 - patients whom underwent neoadjuvant chemotherapy or with recurrent breast cancer, patients with lesions only identified on MRI examination, contraindication to perform MRI, and inadequate tissue sample for IHC examination were excluded from this study.
- Imaging acquisition and analysis are as follows:

I. Mammography

- CC and MLO views were performed using Siemens Mammomat Select.

II. Breast ultrasound

- Handheld bilateral complete ultrasound examination via one of the participating radiologists using a (Philips HD 11) ultrasound system with straight linear array probe (7–12 MHz frequency).

III. DCE–MRI of the breast

- ❖ Using a high field strength (1.5 T MRI system) [Toshiba Excelart Vantage, Japan] and a bilateral breast surface coil with the patient in the prone position.
- ❖ The study was performed in the second week of the menstrual cycle to minimize the amount of background parenchymal enhancement.
- ❖ Imaging acquisition protocol:

A- Localizer

B- Non contrast-enhanced (pre-contrast) sequences/series:

- Axial T1-weighted turbo spin echo (TR/TE = 500/5.3 ms).
- Sagittal and Axial T2-weighted images using turbo spin echo (TR/TE = 120/4.9 ms).
- Axial short time inversion recovery (STIR) (TR/TE = 80/6.5 ms).
- A pre-contrast fat-saturated T2-weighted pulse sequence to separate cysts from solid masses.

C- Contrast-enhanced sequences/series:

- A bolus of contrast (gadolinium-diethylene tri amino penta-acetic acid; Gd-DTPA) (Magnavist, Schering AG Berlin, Germany) was injected manually intravenously at a dose of 0.1 mmol per kilogram body weight (0.1 mmol/kg) followed by saline flush.
- Six dynamic acquisitions were taken: one before and five after intravenous injection of contrast material, using the volume interpolated GRE sequence (T1 High Resolution Isotropic Volumetric Examination) with the parameters (TR/TE = 2.8/9 ms) and slice thickness = 1.5 mm.

D- Post processing:

- Included subtraction, maximum intensity projection (MIP), and creating time/signal intensity curve by placing the region of interest (ROI) at the most enhanced part within the lesion

Interpretation of the imaging studies was performed via one of the participating radiologists, and in cases of interobserver disagreement, the case was discussed, and a joint consensus was reached. The findings were evaluated in accordance with the ACR BI-RADS 5th edition Lexicon (2013).

Tissue sampling and analysis

Percutaneous imaging-guided core biopsy or surgical excision was performed to acquire tumor sample. Specimens underwent immunohistochemistry to detect the levels of ER, PR, HER2 oncogene overexpression, and Ki-67. Stained slides were evaluated for nuclear ER or PR expression according to the College of American Pathologists guidelines ($\geq 1\%$ cutoff for positive) by pathologists. Ki-67 index $< 14\%$ was considered as low expression, and $\geq 14\%$ was considered high expression.

HER2 expression on IHC was based on the cell membrane staining pattern with grade 2+ considered equivocal, grade 3+ considered positive, and grade 1+ or 0 considered negative. All the equivocal samples were further analyzed with fluorescence in situ hybridization where FISH ratio higher than 2.2 or HER2 gene copy greater than 6.0 was considered positive.

Based on ER/PR/HER2 and Ki-67 expression status, breast cancers were categorized into four molecular subtypes in accordance with St. Gallen 2011 consensus surrogate definitions of the molecular subtypes:

- LA subtype
 - ER- and/or PR-positive, HER2-negative, and Ki-67 $< 14\%$
- LB subtype: either
 - ER- and/or PR-positive, HER2-negative, and Ki-67 $\geq 14\%$
 - ER- and/or PR-positive and HER2-positive
- HER2-enriched type (HER2):
 - ER- and PR-negative and HER2-positive
- Triple-negative type (TN):
 - ER, PR, and HER2-negative [12].

Statistical analysis

The data were collected, tabulated, and analyzed by SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Data was summarized using frequency and percentage for qualitative variables, mean, SD, and range for quantitative variables. The imaging features were compared using univariate analyses of data. Comparison between the studied groups was done using Chi-square and Fisher's exact tests for qualitative variables, and Student's *t* test or Mann Whitney *U* test was used for comparing quantitative variables according to distribution of data. *P* (*P* value) less than or equal to 0.05 was considered statistically significant.

Results

This study consisted of 60 patients with a mean age of 56.48 ± 8.70 (range 41–72 years); 44 (73.3%) were HR-positive, 13 (21.7%) were HER2/neu-positive, 34 (56.7%) were LA, 10 (16.7%) were LB, 7 (11.7%) were HER2/neu-enriched, and 9 (15%) were TNBC. Of the luminal B subgroup, 6 cases were HR+ve and HER2neu+ve, while 4 cases were HR + ve, HER2neu-ve, and Ki-67 $\geq 14\%$. In one case, the lesion could not be detected on mammogram due to the extremely dense breast (Table 1).

Imaging features as regard hormonal receptor status (Fig. 1)

On mammographic examination, HR-negative breast cancers were associated with circumscribed margins compared to HR-positive (35.7% vs 8.1%). There was no

Table 1 Descriptive statistics of the studied group regarding age, histological type, HR, HER2neu receptor status, and molecular subtype

		The studied groups N = 60	
Age			
X ± SD		56.48 ± 8.70	
Range		41–72	
		No.	%
Histological type			
IDC	52		86.6
ILC	6		10.0
Medullary	2		3.3
HR			
Positive	44		73.3
Negative	16		26.7
ER			
Positive	44		73.3
Negative	16		26.7
PR			
Positive	34		56.6
Negative	26		43.3
HER2/neu expression			
Positive	13		21.7
Negative	47		78.3
Molecular type			
Luminal A	34		56.7
Luminal B	10		16.7
HER2/neu-enriched	7		11.7
Triple negative	9		15.0

NB: Of the Luminal B subgroup 6 cases were HR+ve and HER2neu+ve, while 4 cases were HR+ve, HER2neu-ve, and Ki-67 ≥ 14%
X mean, SD standard deviation

statistically significant difference as regard the shape of the lesion and the presence of calcifications.

On ultrasound examination, HR-positive breast cancers were significantly associated with posterior acoustic shadowing (77.3%) compared to 37.5% for HR-negative breast cancer cases ($P = 0.004$). Hormonal-negative breast cancers were more likely to be circumscribed compared to the hormonal-positive breast cancers (42.9% vs 7.7%, respectively) ($P = 0.003$). There was no statistical significance as regard the shape of the breast cancer or presence of ultrasonographic-detected calcifications between both groups.

The MRI findings in relation to the hormonal receptor status are summarized in Table 2. Round shape was noted more commonly in HR-negative breast cancers (23.1%) compared to HR-positive breast cancers (2.8%).

HR-negative breast cancers were more likely to present circumscribed margins compared to HR-positive breast cancers (46.2% vs 8.3% respectively). They were also significantly associated with washout kinetics on DCE-MRI (62.5% of hormonal-negative tumors vs 9.1% of hormonal-positive tumors). There was no statistical significance as regard the enhancement pattern.

Imaging features as regard HER2/neu expression (Fig. 2)

The mammographic features in relation to HER2/neu expression in breast cancer are summarized in Table 3. HER2/neu-positive breast cancers were more likely to present calcifications on mammography (69.2%) compared to HER2/neu-negative tumors (25.5%) ($P = 0.007$).

On ultrasound examination, HER2/neu-positive breast cancers were significantly associated with calcifications on sonography (38.5%) compared to HER2/neu-negative breast cancers (8.5%) ($P = 0.02$). There was no statistically significant difference as regards the shape of the lesion, margins, or posterior acoustic features.

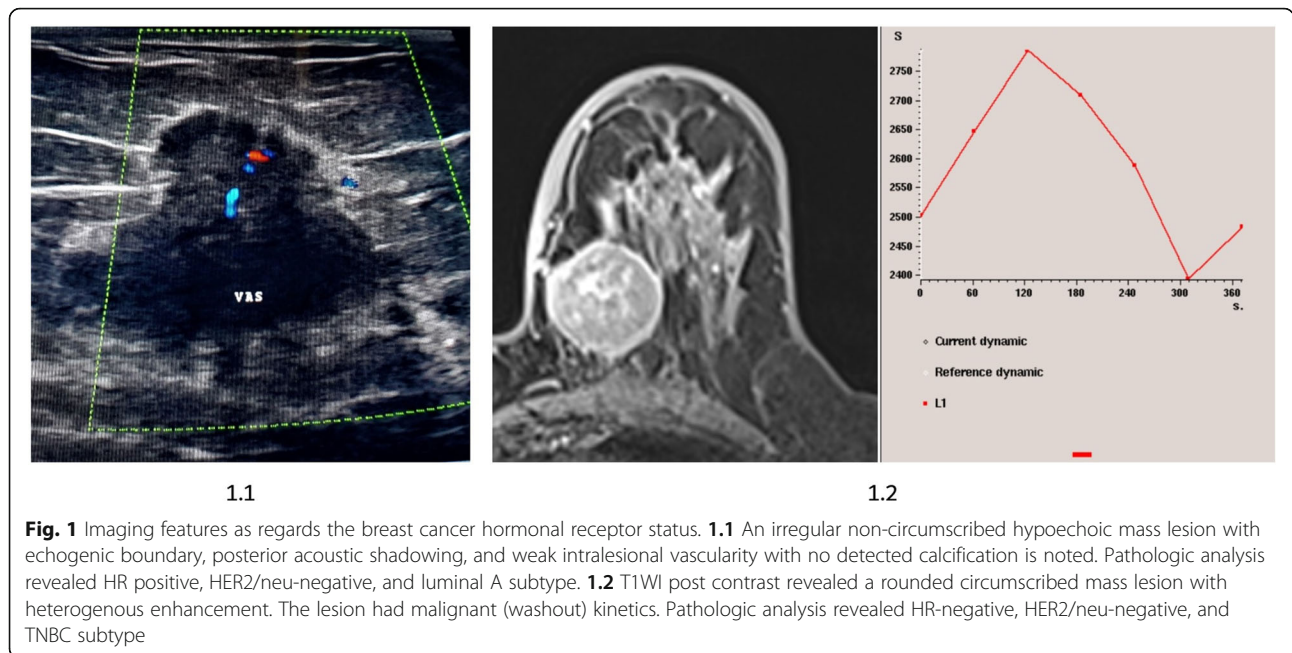
The MRI findings in relation to the HER2/neu expression are summarized in Table 4. HER2/neu-negative breast cancers were more likely to present as mass lesions compared to HER2/neu-positive breast cancers (87.2% vs 61.5% respectively). There was no statistical significance as regard the enhancement pattern, shape, margin, or the enhancement kinetic curves.

Imaging features as regard the molecular subtype (Fig. 3)

On mammography, breast cancers were more often irregular in shape in LB (100%), HER2/neu (100%), LA (70.4%), and TNBC (44.4%) with the TNBC presenting round shape in 2 cases (22.2%) and oval shape in 3 cases (33.3%). TNBC was associated with circumscribed margins (55.6%) ($P = 0.003$). HER2/neu-enriched breast cancers were more likely to present with calcifications which was seen in 5 cases (71.4%) ($P = 0.08$).

On ultrasound examination, there was no statistical significance as regard the shape of the breast cancer within different molecular subtypes. TNBC was more likely to have circumscribed margins (66.7%) ($P < 0.001$) with rounded or oval shape (66.7%) and absent posterior acoustic shadowing (88.9%) on sonographic examination.

The MRI findings of the four molecular subtypes of breast cancer are summarized in Table 5. TNBC were more likely to present rim enhancement pattern (66.7%), whereas heterogenous enhancement pattern was predominant in LA (70.6%), LB (70%), and HER2/neu-enriched (85.7%). TNBC was again shown to be more associated with round shape (33.3%). HER2/neu-enriched and TNBC were significantly associated with washout kinetic curve pattern (57.1% and 66.7% respectively).



Discussion

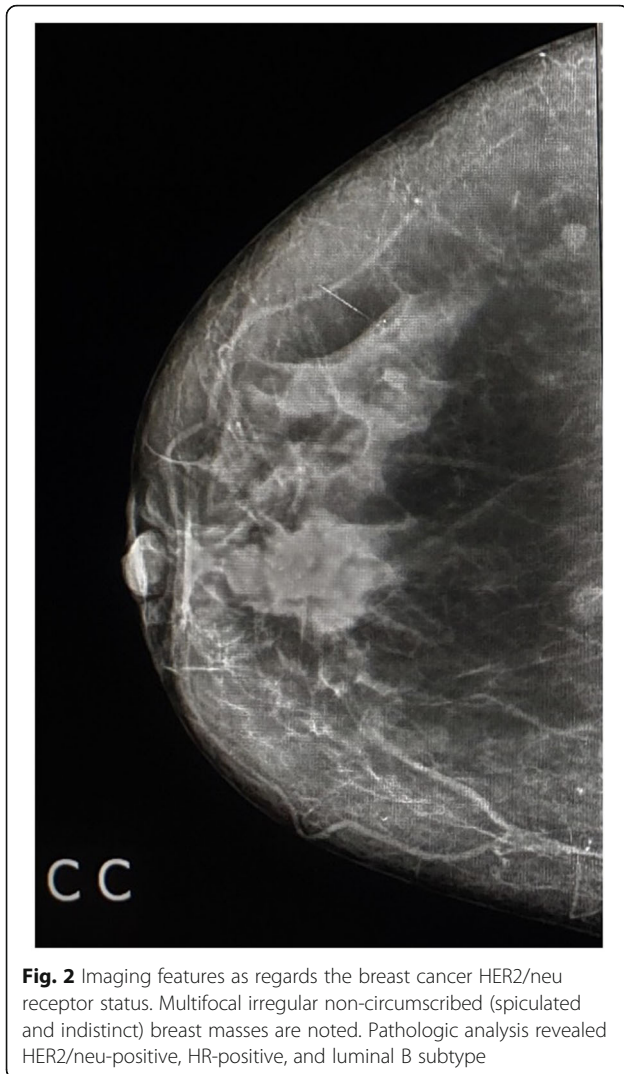
Breast cancer is a diverse group of diseases with different phenotypic and genotypic subtypes. This has significant therapeutic and prognostic effects with the molecular subtyping being an essential therapeutic requirement. Surrogate definitions of the intrinsic molecular subtypes

depend upon hormonal receptor status, HER2neu over-expression, and Ki-67 index. This is usually done via immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH) [12].

In our study, we correlated the hormonal receptor status, HER2neu expression status, and molecular subtype

Table 2 Relationship between hormonal receptors and MRI findings

MRI	HR-positive N = 44		HR-negative N = 16		Test χ^2	P value
	No	%	No	%		
Lesion					Fisher's	
Mass	36	81.8	13	81.2	0.003	1.0
NME	8	18.2	3	18.8		
Enhancement pattern						
Homogenous enhancement	7	15.9	1	6.2		
Heterogenous enhancement	31	70.5	9	56.2	4.52	0.10
RIM enhancement	6	13.6	6	37.5		
Shape of mass lesions						
Round	1	2.8	3	23.1	5.96	0.05
Oval	6	16.7	3	23.1		
Irregular	29	80.6	7	58.2		
Margin of mass lesions					Fisher's	
Circumscribed	3	8.3	6	46.2	9.11	0.007
Non circumscribed	33	91.7	7	53.8		
Kinetic						
Plateau	26	59.1	6	37.5		
Washout	4	9.1	10	62.5	20.46	< 0.001
Persistent	14	31.8	0	0.0		



with imaging features as per mammosonography and MRI.

We found that hormonal-negative tumors were statistically different from hormonal-positive tumors as regards the mass margins, with the hormonal-negative tumors being more circumscribed on mammography, ultrasound, and MRI with a P of 0.03, 0.03, and 0.007 respectively. This was similar to Shin et al. who reported that a circumscribed or microlobulated outline with posterior reinforcement was associated with a high grade and negativity of hormone receptors [13]. Like Song et al. [14], we found no statistically significant difference between hormonal-positive and negative groups as regards the calcification presence, morphology, and distribution. We also found that hormonal-positive tumors were associated with posterior acoustic shadowing in 72.7% of the patients ($P = 0.004$). This was in concordance to Rashmi et al., where they stated that luminal A and luminal B tumors (HR-positive tumors) had a

significant association with non-circumscribed margins and acoustic shadowing ($P < 0.0001$) [15]. According to this study, we found that hormonal-negative tumors are more likely to show malignant DCE kinetics with wash-out curves (62.5% of hormonal-negative tumors vs 9.1% of hormonal-positive tumors, P value of < 0.001). Chen et al. reported similar findings, yet this was not statistically significant according to them ($P = 0.15$) [16]. No statistical significance was found on MRI between hormonal-positive and hormonal-negative tumors as regards the lesion appearance as mass or non-mass enhancement. This was different from Chen et al. results, where they reported that hormonal-negative tumors were more likely to present as non-mass enhancement compared to the hormonal-positive ones ($P < 0.005$) [16]. There was no significant correlation between internal enhancement patterns and the expression of hormonal receptors. This was in concordance with Tao et al. [17].

In this study, 70% of the HER2/neu-positive tumors had calcifications with only 25.5% of the HER2/neu-negative tumors presenting calcifications ($P = 0.007$). This goes in concordance with Sun et al. who reported malignant calcification to be more frequent in HER2/neu-positive tumors ($P = 0.001$) and Boisserie-Lacroix et al. who stated that the presence of calcifications in the mammogram may predict a HER2/neu-positive status when the HER2 score is equivocally 2+ in immunohistochemistry [18, 19].

Elias and colleagues reported that when considering only mass lesions, multifocality was related to increased HER2 overexpression ($P < 0.001$) [1]. This was similar to what we reported on mammographic examination, where HER2/neu-negative was more likely to be unifocal than HER2/neu-positive tumors (92.5% vs 36.4% respectively) ($P < 0.001$). No statistical difference between HER2-positive and HER2-negative as regards the DCE kinetics was noted in this study. This was opposite to Elias et al., where an increased chance of HER2 overexpression was noted with washout or fast initial kinetics on DCE-MRI ($P = 0.01$ and $P < 0.01$ respectively) [1].

Ko et al. found a significant difference between TNBC and non-TNBC as regard the microcalcifications and the focal asymmetries. They reported that TNBC less frequently had associated microcalcifications ($P = 0.0055$), while focal asymmetries were more frequent in the TNBC (22%, $P = 0.003$) [20]. We reported similar findings as regards the less common incidence of microcalcifications in TNBC but not up to a statistically significant level ($P = 0.08$), yet we did not report any case of asymmetry in the TNBC cases. This difference may be due to the smaller number of cases in our study.

In this study, luminal A, luminal B, and HER2-enriched groups were associated with non-circumscribed

Table 3 Relationship between HER2/neu status and mammography findings

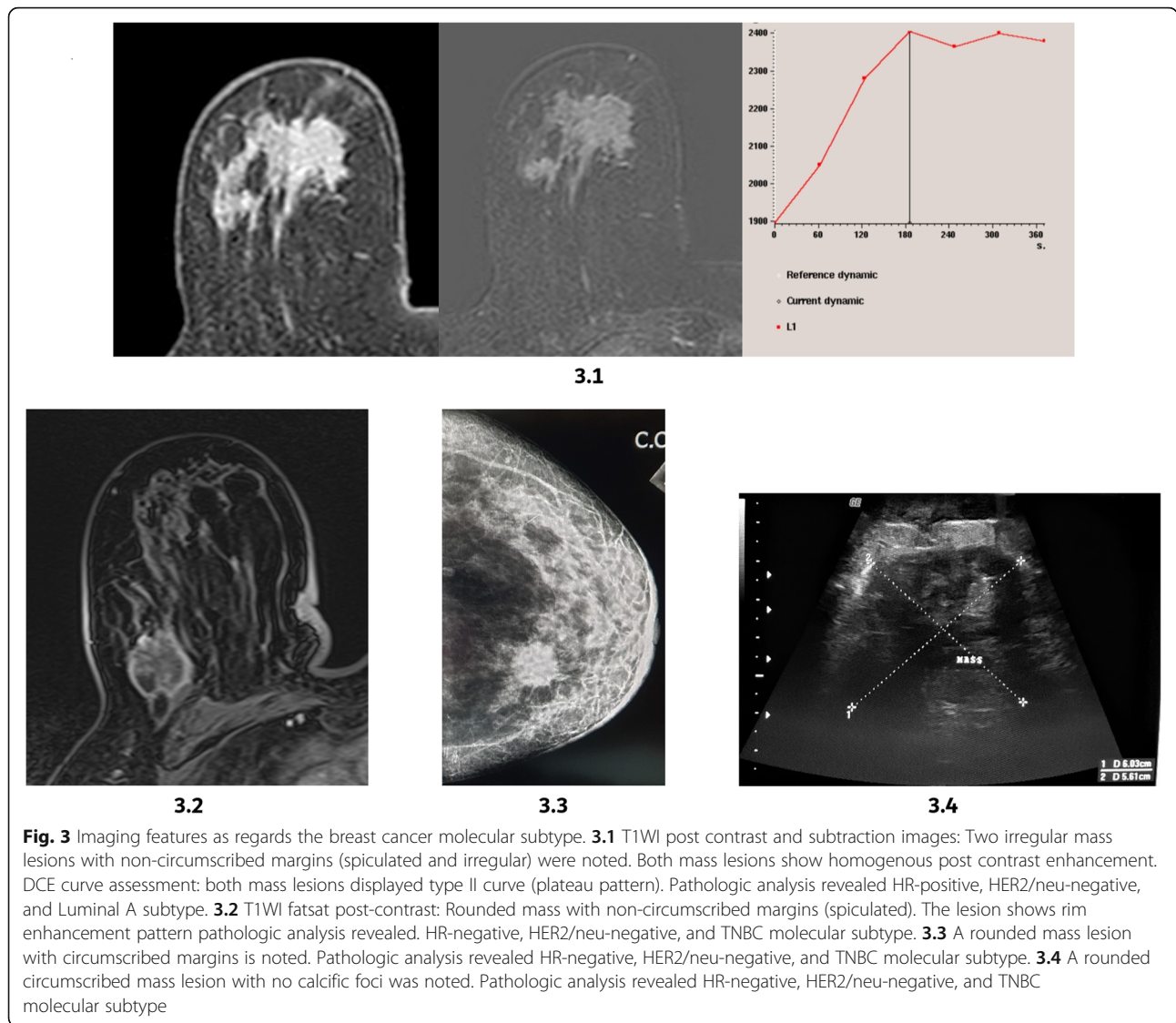
Mammography	HER2/neu-positive N = 13		HER2/neu-negative N = 46		Test	P value
Size					U	
X ± SD	2.14 ± 0.46		2.55 ± 1.09		1.06	0.29
Range	1.2–3.1		1.2–6.5			
	No	%	No	%	χ²	
Lesion						
Mass	11	84.8	40	87.0		
Architectural changes	1	7.7	3	6.5	0.05	0.98
Asymmetry	1	7.7	3	6.5		
Focality of mass lesions					Fisher's	
Unifocal	4	36.4	37	92.5		< 0.001
Multifocal	7	63.6	3	7.5	17.25	
Shape of mass lesions						
Round	0	0.0	4	10.0	4.80	0.09
Oval	0	0.0	9	22.5		
Irregular	11	100	27	67.5		
Calcification					Fisher's	
Present	9	69.2	12	25.5		0.007
Absent	4	30.8	34	74.5	8.55	

χ² = Chi squared test

Table 4 Relationship between HER2/neu receptor status and MRI findings

MRI	HER2/neu-positive N = 13		HER2/neu negative N = 47		Test	P value
	No	%	No	%		
Lesion					Fisher's	
Mass	8	61.5	41	87.2	4.94	0.049
NME	5	38.5	6	12.8		
Enhancement pattern						
Homogenous enhancement	1	7.7	7	14.9		
Heterogenous enhancement	11	84.6	29	61.7	2.45	0.29
Rim enhancement	1	7.7	11	23.4		
Shape of mass lesions						
Round	0	0.0	4	9.8	3.45	0.18
Oval	0	0.0	9	22.0		
Irregular	8	100	28	68.3		
Margin of mass lesions					Fisher's	
Circumscribed	0	0.0	9	22.0	2.15	0.32
Non-circumscribed	8	100	32	78.0		
Kinetic						
Plateau	7	53.8	25	53.2	0.84	0.66
Washout	4	30.8	10	21.3		
Persistent	2	15.4	12	25.55		

Fisher's Fisher's exact test



margins with luminal A and B tumors presenting posterior acoustic shadowing. This was in concordance to Zhang et al. [21].

In this study, all of the TNBC lesions were masses as seen per mammosonography and MRI. This was different from Dogan et al., as they reported mass lesions in 77.3% of the cases and non-mass enhancement in 22.7% of the cases on MRI and mass lesion in 86% of the cases on US [22]. We also reported that TNBC mass lesions on sonography and MRI were associated with circumscribed margins in 66.7% of the cases. This was different from Dogan et al., where they reported that mass lesions on US had circumscribed margins in 21.1% of the masses [22]. Our findings are similar to Ko et al., where they reported on ultrasound examination that 86% of the TNBC presented as masses and significantly had circumscribed (57%) as opposed to non-circumscribed margins [20].

We also reported a significant difference between TNBC and other molecular subtypes regarding the internal enhancement pattern of mass lesions; rim internal enhancement was predominant in TNBC mass lesions in this study compared to the predominant heterogenous enhancement pattern in the other subtypes. This may be attributed to increased tumoral necrosis in TN breast cancers. Our results were consistent with Azzam et al. and Youk et al., where they reported similar results ($P = 0.001$ and $P < 0.0001$, respectively) [23, 24]. Teifke et al. noted that rim enhancement is usually associated with high-grade tumors and is considered the most useful MR imaging feature for identifying TN cancers [25].

The major limitation of this study was a relatively small number of patients. Another limitation is the interobserver variability in reporting the different lesions which is likely to cause some variability in the results

Table 5 Relationship between molecular subtypes and MRI findings

MRI	Luminal A N = 34		Luminal B N = 10		HER2/neu-enriched N = 7		Triple negative N = 9		Test X ²	P value
	No	%	No	%	No	%	No	%		
Lesion										
Mass	28	82.4	8	80	4	57.1	9	100	4.86	0.18
NME	6	17.6	2	20	3	42.9	0	0.0		
Enhancement pattern										
Homogenous enhancement	5	14.7	2	20.0	1	14.3	0	0.0		
Heterogenous enhancement	24	70.6	7	70.0	6	85.7	3	33.3	15.74	0.02
Rim enhancement	5	14.7	1	10.0	0	0.0	6	66.7		
Shape of mass lesions										
Round	1	3.6	0	0.0	0	0.0	3	33.3	13.34	0.03
Oval	5	17.9	1	12.5	0	0.0	3	33.3		
Irregular	22	78.6	7	87.5	4	100	3	33.3		
Margin of mass lesions										
Circumscribed	2	7.1	1	12.5	0	0	6	66.7	17.44	0.001
Non circumscribed	26	92.9	7	87.5	4	100	3	33.3		
Kinetic										
Plateau	20	58.8	6	60.0	3	42.9	3	33.3		
Washout	3	8.8	1	10.0	4	57.1	6	66.7	20.7	0.002
Persistent	11	32.4	3	30.0	0	0.0	0	0.0		

reported by different investigators. It is worth noting that possibility of intratumoral heterogeneity especially in the case where the histopathological assessment was via core biopsy may contribute to discordance in ER, PR, and HER2 status, with possible implications for breast cancer subtype classification.

Conclusion

This study showed that tumor's margins, microcalcifications on mammography, posterior acoustic features on ultrasonography, enhancement pattern, and kinetics on MRI strongly correlate with hormonal receptor status, HER2neu expression, and molecular subtype. Hormonal-positive tumors tend to be of non-circumscribed margins with posterior acoustic shadowing on ultrasonography. HR-negative tumors tend to be larger, more commonly associated with circumscribed margins and present with washout kinetics on MRI. HER2neu-positive tumors tend to present microcalcifications. TNBC is usually circumscribed masses with washout kinetics on MRI.

Abbreviations

HR: Hormonal receptor; US: Ultrasonography; MRI: Magnetic resonance imaging; FISH: Fluorescence in situ hybridization; DCE: Dynamic contrast enhancement; TNBC: Triple-negative breast cancer; IHC: Immunohistochemistry; ER: Estrogen receptor; PR: Progesterone receptor; CC: Craniocaudal; MLO: Medial lateral oblique; GRE: Gradient-recalled echo; MIP: Maximum intensity projection; ROI: Region of interest

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Availability for data and materials

Data will be available upon request via contacting the corresponding author.

Authors' contributions

MA, AE, AA, and WM contributed equally to study design, data collection, analysis, and interpretation of results. All authors read and approved the final manuscript

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Ethics approval and consent to participate

All study procedures were conducted in accordance with the declaration of Helsinki and were approved by the ethical committee under the supervision of Prof. Dr. Walaa Farid and the Menoufia Faculty of Medicine Council, reference number 3/86/1/9/2016. All data were extracted after taking fully informed written consent from each patient involved in the study after explanation of the procedures and the importance of the study, and the confidentiality of the patient's data was guaranteed.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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