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Contrast Enhanced Mammography for the Non-Invasive Differentiation of Breast Cancer Molecular Subtypes and Tumor Grade

BASMA M. ALKALAAWY, M.D.*; OMNIA GOHAR, M.Sc.*; PASSANT E. SHIBEL, M.D.** and MARIAM RAAFAT, M.D.*

The Department of Diagnostic & Interventional Radiology and Department of Pathology**, Faculty of Medicine, Cairo University*

Abstract

Background: Breast cancer is a heterogenous disease with different molecular subtypes. Each molecular subtype has its own prognosis and management. Identifying this molecular subtype is necessary to allow individualized patient treatment. CESM has the potential to non-invasively differentiate the various molecular subtypes of breast cancer. In this manner it can provide information about the tumoras a wholenot just the biopsied part of the tumor.

Aim of Study: Assess Contrast enhanced spectral mammography as a non-invasive imaging tool in predicting molecular subtypes of breast cancer and tumor grade.

Patients and Methods: This study includes 95 female patients with 98 breast lesions in the time period from January 2021 to February 2022. All breast lesions were assessed by Digital mammography and ultrasound, followed by contrast mammography. Biopsy was then performed (BIRADS 4&5) to identify the pathologic type and tumor grade followed by immunohistochemistry to identify the molecular subtype of each tumor.

The dominant feature of each molecular subtype on contrast mammography was recorded regarding lesion morphology (mass/distortion/asymmetry/pathological microcalcification/lesion margins) and pattern of enhancement.

Results: Chi square (χ^2) test shows a significant association between lesion margins and the various molecular subtypes of breast cancer (p=0.014). It also shows a significant association between molecular subtype and tumor grade (p=0.018). However, the enhancement pattern didn't reflect a significant association to the molecular subtypes (p=0.101 for mass enhancement and 0.419 for NME).

Key Words: *Breast cancer – Molecular subtypes – Contrast enhanced mammography – Contrast enhanced spectral mammography.*

Correspondence to: Dr. Basma Mohamed Alkalaawy, The Department of Diagnostic & Interventional Radiology, Faculty of Medicine, Cairo University

Introduction

AMONG female cancers, breast cancer has the highest incidence and death rates. In 2020, the newly diagnosed cases of breast cancer reached 2.3 million cases globally (11.7% of all female cancers) that resulted in 685,000 cancer related deaths. Economically struggling countries such as sub-Saharan Africa show the highest disease burden **[1]**.

Full field digital Mammography (FFDM) is the baseline diagnostic and screening tool for breast lesions in most cases. However, being a 2D imaging modality it has its limitations especially dense breast tissues. Contrast enhanced spectral mammography (CESM) was introduced for clinical use in 2011 with the aim of overcoming some of the drawbacks of mammography. It combines anatomical and functional data to highlight breast pathol-

Abbreviations:

CESM	: Contrast enhanced spectral mammography.
FFDM	: Full field digital mammography
LE	: Low energy
HR	: Hormonal receptor
ER	: Estrogen receptor
PR	: Progesterone receptor
HER2	: Human epidermal growth factor receptor 2
TN	: Triple negative
AJCC	: American Joint Committee on Cancer
US	: Ultrasound
CC	: Craniocaudal
MLO	: Mediolateral oblique
NME	: Non-mass enhancement
IHC	: Immunohistochemistry
ACR	: American college of radiology
IDC	: Invasive duct carcinoma
IMC	: Invasive mammary carcinoma
ILC	: Invasive lobular carcinoma
NST	: No specific type
Ki-67	: Cell proliferation marker/mitotic index

ogy. The LE images of CESM provide similar information to 2D mammography and the subtraction images only show the intended breast lesion [2].

Breast cancer prognosis is not limited by the anatomic extent of disease spread but it also includes tumor grade, and immunohistochemistry biomarkers especially ER, PR, HER2, and multigene assays. Since 2018 AJCC staging system for breast cancer has adopted a new staging system incorporating these factors with the aim of providing individualized treatment and improved patient care [3].

According to AJCC system, the molecular subtypes of breast cancer are mainly four groups, that reflect distinct tumor behavior and prognosis. They are; Luminal cancers (Luminal A&B) which are hormone receptor positive (ER+, PR+/-), HER2 (human epidermal growth factor receptor-2) enriched, and Triple negative (negative for ER, PR, and HER2) cancers. ER+ and PR+ tumors benefit from endocrine therapy. Luminal cancers, especially Luminal A, carry the best prognosis amid the different molecular subtypes. However, Luminal B may show slightly higher recurrence rate. On the other hand, HER2- enriched and TN cancers are more aggressive, with higher recurrence rates and don't benefit from hormonal treatment [4].

The purpose of this study is to evaluate the specific morphology and enhancement pattern on CESM in relation to different molecular subtypes of breast cancer and tumor grade. Our aim is to find enough imaging features of each subtype that can aid in the noninvasive diagnosis of breast cancer lesions.

Patients and Methods

Patients:

This study was conducted on 95 females, with 98 breast lesions during the period from January 2021 till February 2022 at The Department of Radiology Faculty of Medicine. Patients presented to our institute with either breast complaint or for screening (BIRADS 4 &5 lesions). We also included patients with pathologically proven breast cancer presenting for assessment of disease extent (BIRADS 6). Our study included Female patients above 18 years old with so no-mammography identified lesions that are classified as (BIRADS 4, 5 and 6).

Exclusion criteria: Patients who were pregnant, lactating, with known allergic reaction to contrast media or renal disease. Also, patients who had any form of therapeutic intervention whether surgical or neoadjuvant medical treatment were excluded from our study.

Methods:

Each patient underwent Standard 2D mammography with Complementary 2D US Examination. Afterwards, Lesions identified as BIRADS 4 and 5 underwent CESM. This was followed by ultrasound guided Tru-cut biopsy and histopathological analysis was then performed. Patients with BIRADS 6 lesions undergone only CESM. Pathological type and molecular subtype of each cancer patient was determined. Correlation between the CESM features and each molecular subtype was finally done.

Standard 2D Mammography technique:

Mammography was carried out using Senographe 2000 D full field digital mammography Essential GE Healthcare. Each breast was imaged in the standard two projections (CC and MLO views). The observed findings include presence of a mass, focal asymmetry, architectural distortion, lesion extensions, calcifications, number of lesions & skin infiltration.

CESM technique:

CESM was achieved using the same Senographe 2000 D full field digital mammography Essential GE Healthcare (the same used for FFDM acquisition) with special software adaptation to enable contrast visualization.

Before breast compression, a single-shot intravenous injection of an iodinated contrast agent (300mg iodine/ml, 1.5ml/kg BW minimum 50ml, maximum 120ml) was given to the patient while seated. After two minutes, both breasts are imaged in the standard CC and MLO views. Each view consists of two exposures, one below (<32kVp) and one above the k-edge of iodine (<49kVp). Afterwards, the low- and high-energy images were processed to abolish parenchymal background and show only the pathological uptake of contrast agent.

Two independent radiologists specialized in breast imaging with at least 10 years of experience in the field of mammography and CESM reviewed the CESM images. The readers were provided no information regarding other imaging and clinical findings.

Image interpretation:

Lesion morphology was assessed on the LE image of CESM (that resembles FFDM) and the subtracted images. Lesion margins are more conspicuous on subtracted CESM images. On the subtracted images the lesions were reported regarding pattern of enhancement, as well as morphology. The lesions identified on CESM were categorized according to the classification system adopted by Kamal et al., 2016 and using the MRI BI-RADS lexicon. The three main categories are:

Focus: Enhancement less than 5mm. A focus was considered malignant if it is single, unilateral or intensely enhancing.

Mass: 3D space-occupying lesion. A mass was considered malignant if it is irregular/spiculated and showing heterogeneous/rim enhancement.

Non-mass: (NME) is non-space occupying enhancement. This type is considered malignant if it is asymmetric, adopting a focal, linear, segmental or regional distribution and when the internal pattern of enhancement is either heterogeneous, clumped or clustered ring.

Pathology technique:

The histopathological examination was carried out at the Pathology Department, Cairo University. Tissue biopsies were processed in paraffin blocks, from which Hematoxylin and Eosin (H&E) stained sections were prepared for confirmation of malignancy and tumor grading. Subsequently immunohistochemical staining (IHC) was performed with specific antibodies to identify the hormonal receptors of the lesions (ER, PR) HER2 gene expression and Ki-67.

Following the classification system suggested by Fragomeni et al., the molecular subtype was determined by the following criteria:

- Luminal A: ER+, PR+, HER2_, and low Ki-67 index.
- Luminal B: (HER2–): ER+, PR+ or PR–, HER2–, and high Ki-67 index.
- Luminal B: (HER2+): ER+, PR+, HER2+.
- HER2: ER–, PR–, HER2+.
- Triple-negative: ER–, PR–, HER2–.

Molecular subtype	ER		PR	HER2
Luminal A	Positive	and/or	Positive	Negative
Luminal B	Positive	and/or	Positive or negative **a**	Negative
Luminal B	Positive	and/or	Positive or negative **b**	Positive
HER2	Negative		Negative	Positive
Triple negative or basal-like	Negative		Negative	Negative

Abbreviations: ER: Estrogen receptor. HER2: Human epidermal growth factor receptor 2. PR: Progesterone receptor. **a** (PR <20% + Ki 67 >14%). **b** (Any PR + any Ki 67).

Fig. (1): Classification of molecular subtypes and correlation with biomarker staining on immunohistochemistry **[4]**.

Statistical methods:

Patients' demographic data as well as pathology and tumor grade were summarized using mean, standard deviation, minimum and maximum in quantitative data. Frequency (count) and relative frequency (percentage) were used for each categorical data. For correlating CESM findings to molecular subtypes, Chi square (χ^2) test was performed. *p*-values less than 0.05 were considered as statistically significant.

Results

Our study included 95 female patients with 98 (BIRADS 4,5 and 6) breast lesions. DM, CESM and US guided Tru-cut biopsy were performed for BIRADS 4&5 lesions, whereas CESM only was performed for BIRADS 6 lesions. For the masses proved to be malignant pathologically; IHC was carried out to assess the molecular subtype.

The age of the patients ranged from 29 to 72 years old with mean age 49.79 and SD ±11.53. Regarding the breast density; 52 cases were ACR B (53.1%), 43 cases were ACR C (43.9%) and 3 cases were ACR D (3%). Regarding BIRADS classification; 23 (36.7%) cases were BIRADS 4, 43 (43.8%) cases were BIRADS 5, and finally 19 (19.4%) cases were BIRADS 6. The pathological type, tumor grade and molecular subtypes are illustrated in Table (1).

Table (1): Showing the distribution of patients according to pathological type, tumor grade and molecular subtype.

	Count	%
Pathological types:		
IDC	82	83.7
ILC	8	8.2
IMC	7	7.1
High grade pleomorphic carcinoma (uncommon variant of NST)	1	1.0
Pathological grade:		
1	6	6.1
2	67	68.4
3	25	25.5
Molecular subtypes:		
Luminal A	35	35.7
Luminal B	41	41.8
HER2 overexpression	12	12.2
TN	10	10.2

On FFDM and CESM lesions were assessed for the presence of masses, architectural distortion/ asymmetry, pathological microcalcifications, and pattern of enhancement. The distribution of the lesions is illustrated in Table (2).

Tumor Grade VS mass lesion margins:

Low grade tumors (grade 1) mostly had spiculated margins, while higher grade tumors (grade 2 & 3) had irregular or circumscribed/lobulated margins. This is illustrated in Table (3).

Molecular subtypes: nature of the lesion, tumor grade, lesion margins and pattern of enhancement:

Table (4) shows the lesion distribution in the various molecular subtypes.The most common presentation among all molecular subtypes was mass lesion. The highest percentage of asymmetry/ distortion was evident in HER2 enriched cancers. On the other hand, TN tumors presented only as mass lesions (100%). Pathological microcalcifications was present in 50% of HER2+ cases, while TN cancers showed no pathological calcifications. Grade 1 tumors were mostly luminal A cancers (83.3%), while higher grade tumors were luminal B, HER2 enriched, and TN cancers as illustrated in Table (5).

Luminal cancers mostly had irregular/spiculated margins. Although, Luminal A lesions showed slightly higher percentage of spiculated margins (46.7% VS 42.9%) where as Luminal B showed higher percentage of irregular margins (51.4% VS 50%). The highest percentage of circumscribed/ lobulated margins was evident in TN. This is illustrated in Table (6).

Most evident pattern of enhancement among all molecular subtypes was mass enhancement, particularly heterogenous mass enhancement. Lesions that presented with architectural distortion/ asymmetry in mammography elicited heterogenous or clumped non mass enhancement. Rim enhancement was evident in high grade tumors particularly Luminal B and TN tumors. The pattern of enhancement in relation to the molecular subtype is illustrated in Table (7).

Table (2): Showing the mammographic and CESM findings of the 98 breast cancer lesions.

	Count	%
Mass lesion:		
Mass	84	85.7
No Mass	14	14.3
Mass margin:		
Spiculated	30	35.7
Irregular	47	56.0
Circumscribed	4	4.8
Lobulated	3	3.6
Architectural distortion/asymmetry:		
Yes	14	14.3
No	84	85.7
Microcalcifications:		
Yes	19	19.4
No	79	80.6
Pattern of enhancement:		
Heterogenous	86	87.8
Homogenous	7	7.1
Clumped	1	1.0
Rim	4	4.1
Non mass enhancement:		
Yes	13	13.3
No	85	86.7

	Pathological grade						X^2	*p*-value
	1		2		3			
	Count	%	Count	%	Count	%		

	Count	%	Count	%	Count	%	Count	%

	Count	%	Count	%	Count	%	Count	%

	Count	%	Count	%	Count	%	Count	%		
Mass margin:										
Spiculated	14	46.7	15	42.9	1	11.1	0	0.0	16.908	0.014
Irregular	15	50.0	18	51.4	7	77.8	7	70.0		
Circumscribed	0	0.0	1	2.9	1	11.1	2	20.0		
Lobulated	1	3.3	1	2.9	0	0.0	1	10.0		

Table (7): Illustrating the pattern of enhancement in the different molecular subtypes.

	Molecular subtypes								X^2	*p*-value
	Luminal A		Luminal B		Her2 overexpression		TN			
	Count	%	Count	%	Count	%	Count	%		
Pattern of enhancement:										
Heterogenous	31	88.6	37	90.2	10	83.3	8	80.0	14.416	0.101
Homogenous	4	11.4	2	4.9	1	8.3	0	0.0		
Clumped	0	0.0	0	0.0	1	8.3	0	0.0		
Rim	0	0.0	2	4.9	0	0.0	2	20.0		
Non mass enhancement:										
Yes	4	11.4	6	14.6	3	25.0	0	0.0	3.135	0.419
No	31	88.6	35	85.4	9	75.0	10	100.0		

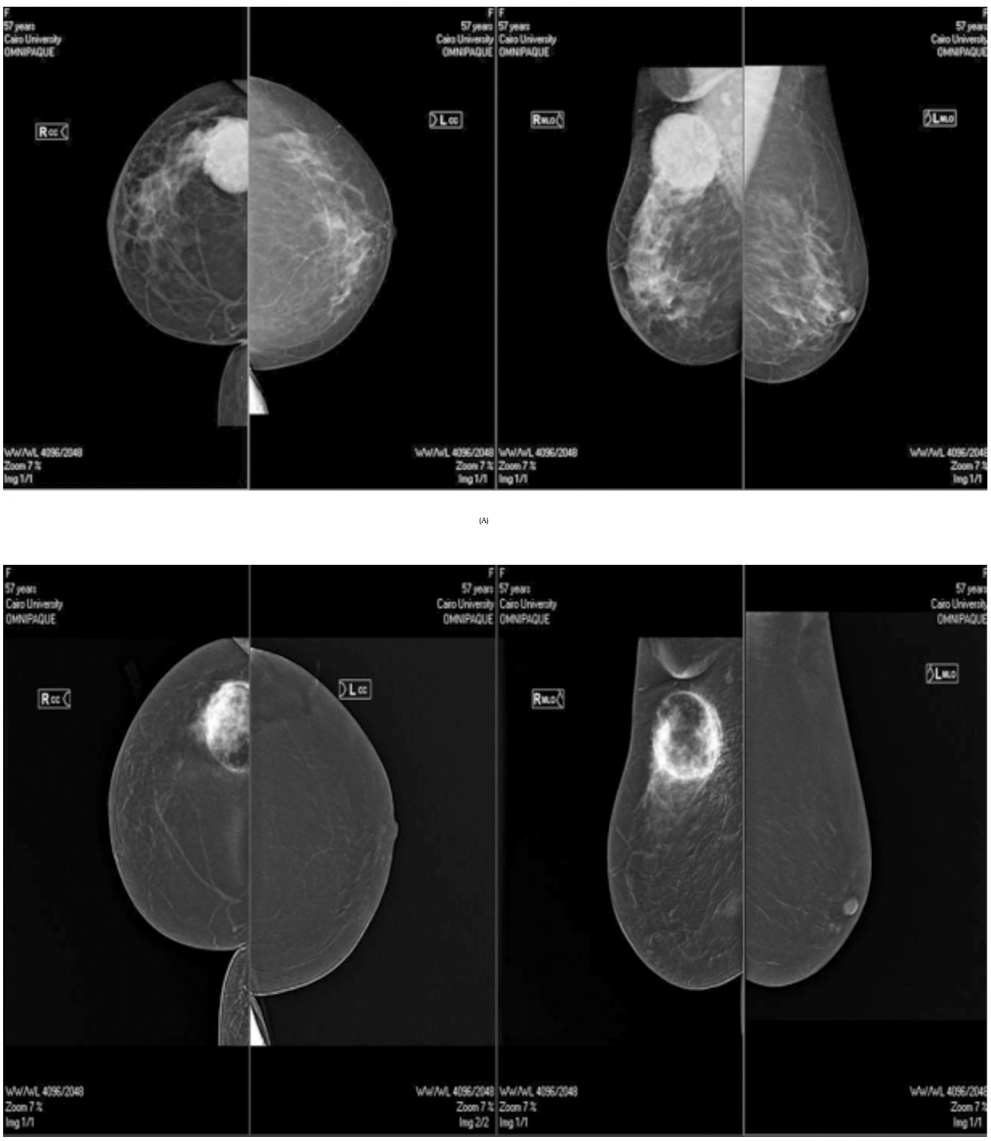
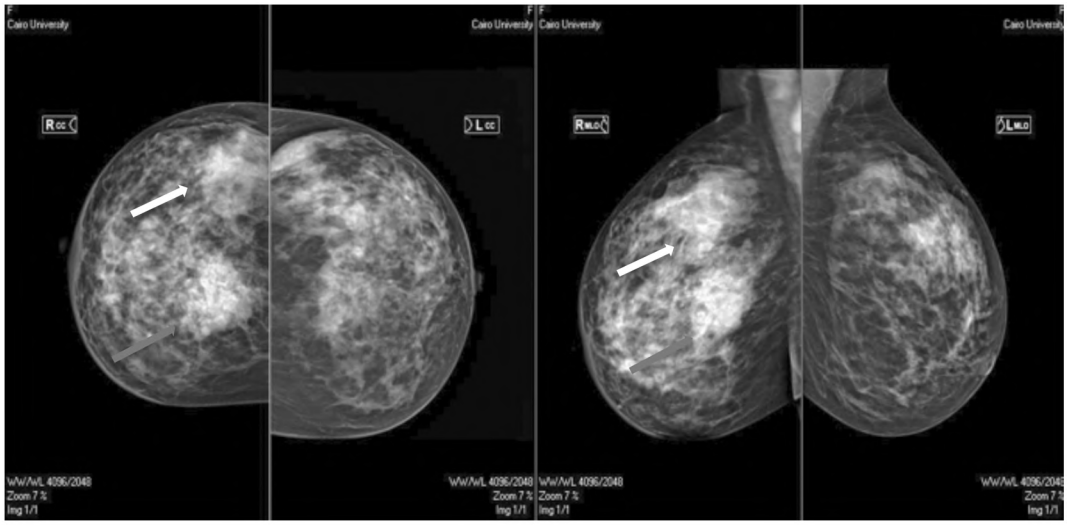
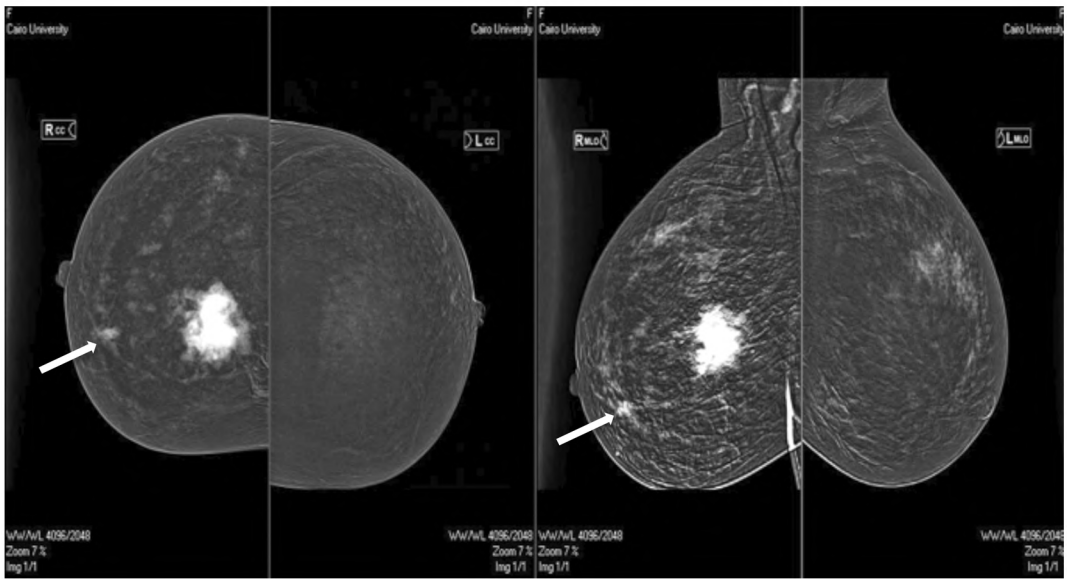


Fig. (2): (A): DM in CC & MLO viewsof a 57-year-old patient presenting with right breast lump. It reveals right UOQ circumscribed mass. (B): CESM of the same patient revealing right UOQ rim enhancing lesion with areas of internal heterogeneous enhancement.

Pathology: IDC, Grade 3, Molecular subtype: Triple negative (TN), ER-ve, PR-ve, HER2 -ve, Ki67=80%.



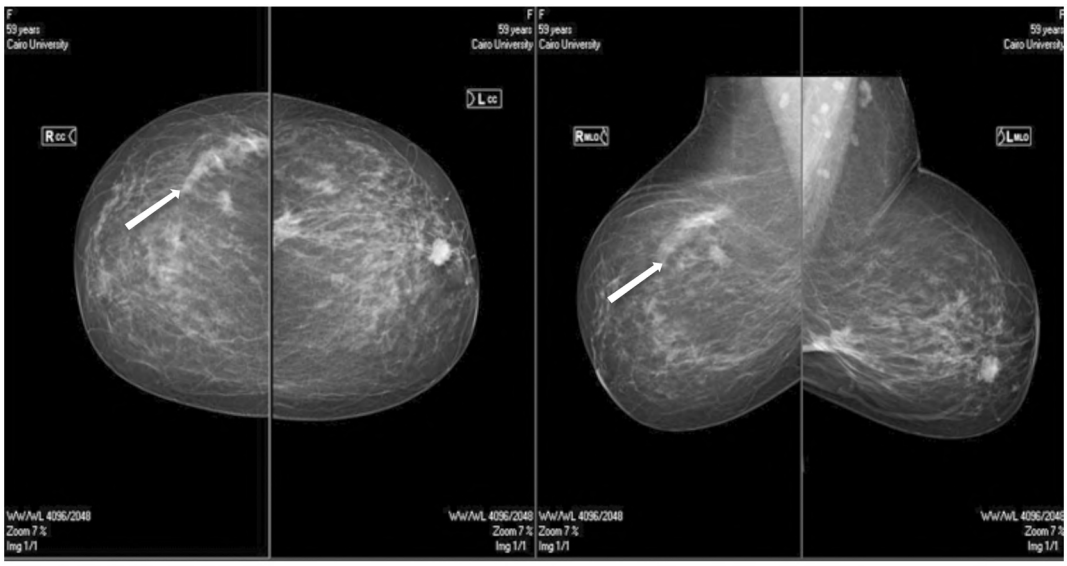
(A)



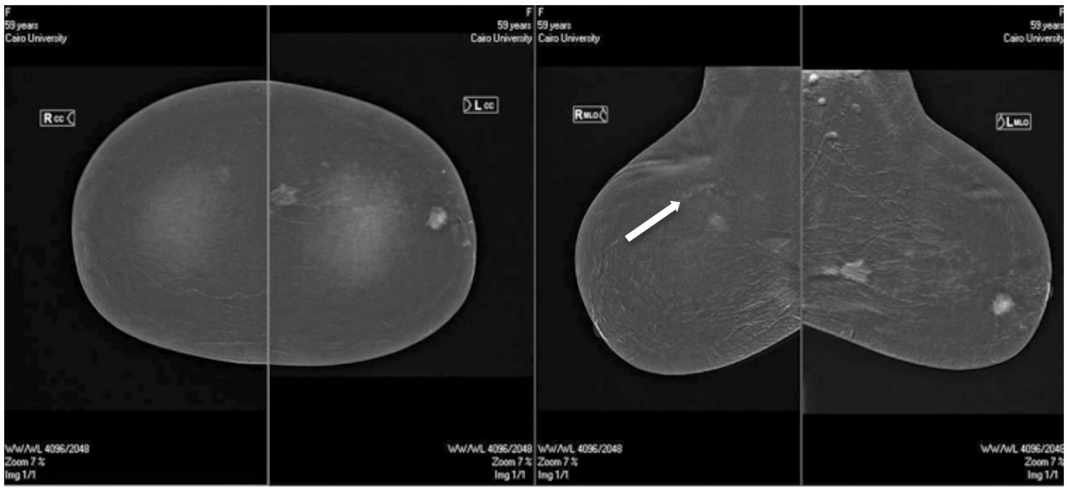
(B)

Fig. (3): (A): DM in CC & MLO views, of 50-year-old patient presenting with right breast lump. It shows right UIQ irregular high density mass lesion with overlying pathological grouped pleomorphic and amorphous calcifications (blue arrow) as well as UOQ area of focal asymmetry (white arrow). (B): CESM of the same patient showing moderate background parenchymal enhancement and Right UIQ irregular heterogeneously enhancing mass lesion, corresponding to the UIQ lesion detected on DM. A similar, yet much smaller lesion is seen anterior to the forementioned one (white arrow). The area of right UOQ focal asymmetry shows no pathological enhancement. It shows rather bilateral UOQ symmetrical background enhancement. Pathology: IDC, Grade 2

Molecular subtype: HER-2 overexpression; ER -ve 0/8, PR +ve 8/8, HER2 +ve (+3), KI 67=80%.



(A)



(B)

Fig. (4): (A): DM in CC & MLO views of 59-year-old female patient presenting with left breast lump. It reveals Left LOQ two spiculated mass lesions as well as right UOQ spiculated mass lesion with associated focalasymmetry (white arrow). (B): CESM of the same patient revealing spiculated heterogeneously enhancing mass lesions corresponding to the mass lesions noted on DM The focal asymmetry noted on the right side shows faint heterogenous non mass enhancement (white arrow), evident in MLO view.

Pathology:
Left breast: IDC Grade1, Molecular subtype: Luminal A : ER +ve 8/8, PR +ve 8/8,
HER2 -ve (0) and Ki67=5-10%
Right breast: IDC Grade 2, Molecular subtype: Luminal A: ER +ve 8/8,PR +ve 8/8,
HER2 -ve (0), Ki67=10%.

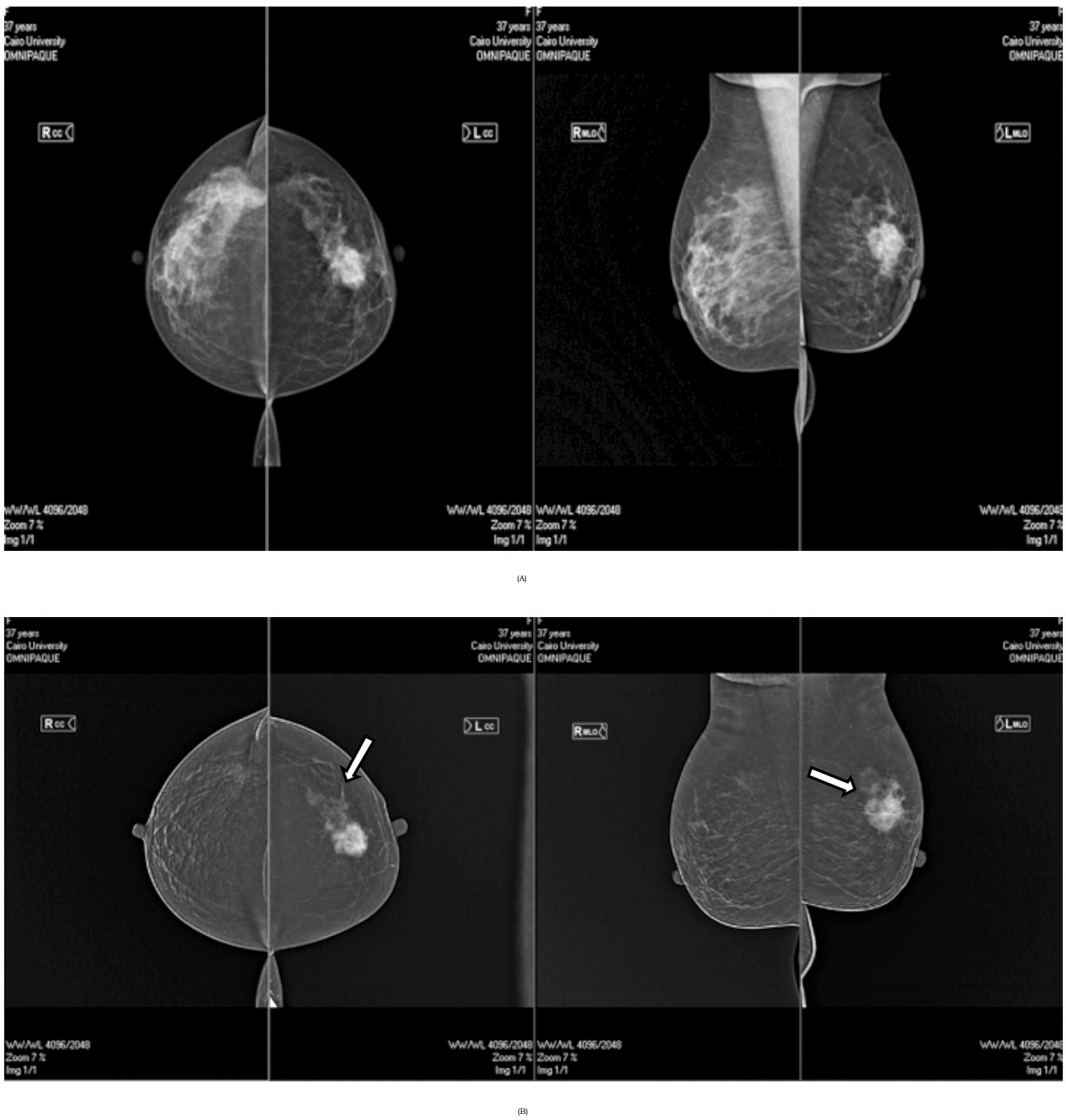


Fig. (5): (A): DM in CC & MLO views of 37-year-old female complaining of left breast lump. It shows Left upper central irregular dense lesion with associated nipple retraction and mild skin thickening. (b): CESM of the same patient revealing irregular heterogeneously enhancing mass lesion corresponding to the mass lesions noted on DM, with contiguous non mass enhancement (white arrow).

Pathology: IDC, Grade 2, Molecular subtype: Luminal B: ER +ve 8/8, PR +ve 8/8, Her2 neu +ve (+3), KI67 <10%.

Discussion

Around the world, breast cancer is one of the most commonly diagnosed cancers. It's also a leading cause of female cancer related fatalities **[5]**. Digital mammography +/- US remain the cornerstone for breast cancer diagnosis and staging. However, its limited sensitivity in dense breasts has given way to the emergence of advanced techniques such as CESM.The sensitivity and specificity of CESM can reach up to 85% & 77% respectively **[6]**.

Estrogen receptors (ER), progesterone receptors (PR), HER2 (Human epidermal growth factor receptor 2), and cell proliferation marker (Ki-67), determine the molecular subtype of breast cancer. These subtypes are Luminal A, Luminal B, enriched HER2 (HER2+), and Triple Negative (TN) cancers **[7]**. They play an integral part in the diagnosis of breast cancer. They reflect different tumor behavior, prognosis and treatment **[8]**.

Although invasive tissue sampling remains the standard of diagnosis of histologic type, tumor grade and molecular subtype it's subject to sampling selection bias and doesn't provide adequate representation of the tumor in its entirety. Therefore, there is an ongoing need for the non-invasive comprehensive diagnosis of breast cancer biology, especially molecular subtypes **[9]**.

In the present study Grade 1 tumors were spiculated in 83.3% of the cases, while Grade 2 and 3 tumors were mostly irregular. Grade 2 tumors were irregular in 61.7% of the cases and Grade 3 tumors were irregular in 50% of the cases. Circumscribed/ lobulated margins were noted with high grade tumors. Spiculated margins were seen only in luminal cancers, while circumscribed margins were seen with the higher-grade tumors especially TN cancers.

This comes in agreement with Ambicka et al., (who studied tumor borders on CESM). They didn't find a significant relationship between tumor margins and tumor grade (p=0.98 in their study vs p=0.141 in our study). Similarly, Huang et al., who studied the relation between MRI features and tumor grade suggested that lesion margins didn't reflect the WHO pathological grade (p>0.05). However, Lacroix et al., concluded that spicules were most often noted with low grade cancers particularly Grade 1 unlike the deceivingly benign circumscribed margins in Grade 2 & 3 cancers. It has been suggested that spiculated cancers have more favorable prognosis. Spiculations usually result from the relatively slow invasion into the surrounding breast parenchyma thus providing sufficient time for the body defensive mechanisms to produce enough connective tissue around malignant cells limiting their spread **[10-12]**.

Our study concluded significant association between Molecular subtypes and tumor grade (p=0.018). Low grade cancers or grade 1 cancers were mostly Luminal A (83.3%). Luminal B, HER2+ and TN cancers were mostly grade 2 and 3. L. NavarroVilar et al., concluded similar results.They found that TN cancers were mostly high grade (76.5%), while Luminal B and Her2+ were moderate grade and Luminal A cancers were low grade **[13]**.

Most studies discussing enhancement of molecular subtypes are MRI based with few studies addressing the role of CESM. But since we applied MRI based morphological descriptors in our methodology, these MRI based studies were used to verify our results.

Lesion margins tend to be more evident on CESM than DM. In CESM there is suppression of the background parenchyma which highlights the lesion only, without the tissue overlap encountered during FFDM. In the present study we found a significant association between the lesion margins and the different molecular subtypes of breast cancer (p=0.014). However, the pattern of enhancement itself was not specific for each molecular subtype (p=0.101 for mass lesions and p=0.419 for non-mass enhancement). That being said, the patterns of enhancement observed in our study are compliant with several studies discussing the enhancement of the different molecular subtypes of breast cancer.

In the current study, Luminal A and B cancers presented mostly as irregular mass lesions (85.7% and 85.4% respectively) with spiculated (46.7% for Luminal A and 42.9% for luminal B) or irregular (50% for A and 51.4% for B) margins and heterogenous enhancement (88.6% for A and 90.2% for B). Architectural distortion was higher in luminal A than B cancers (17.1% vs 12.2% respectively). Pathological calcification was slightly higher in Luminal B than A cancers (22% VS 11.4% respectively). These results come in concordance with several studies **[9,10]**. They suggested that spiculated margins were significantly higher in Luminal A cancers than other subtypes. Architectural distortion was also more evident with luminal A cancers. L.NavarroVilar et al, who studied breast cancer molecular subtypes on MRI, also reported that Luminal cancers usually presented with mass like enhancement and had irregular margins. Whereas, HER2+ enriched cancers showed more non-mass like enhancement **[13]**.

Spiculations seem to be a main feature of luminal cancers, particularly luminal A **[14]**. T. Kazama et al., explained that HR+ cancers tend to show more stromal reaction and fibrosis which contribute to the irregular margins and heterogenous internal enhancement **[17]**. J. Huang et al., concluded that Luminal cancers are usually associated with spiculated margins. This may be due to the fact that HR+ (hormonal receptors) tumors elicit pronounced fibrosis into the surrounding tissues. Similar to our study, they also reported higher incidence of microcalcifications in Luminal B than A tumors **[18]**.

We found that the most frequent enhancement pattern in Luminal cancers was heterogenous mass enhancement (88.6% for subtype A and 90.2% for subtype B). This conforms with the meta-analysis study performed by K Johnson et al., which concluded that Luminal cancers usually give rise to irregular enhancing masses and less commonly non-mass enhancement **[19]**. L. Grimm et al., advocated that homogenous enhancement had 100% negative predictive value to Luminal B cancers **[20]**.

In the present study Her2+ enriched tumors were high grade. They presented as a mass lesion in 75% and as area of symmetry/distortion in 25% of the cases. Pathological microcalcifications were evident in 50% of lesions ($p<0.05$). Mass lesion margins were mostly irregular (77.8%) and eliciting heterogenous mass enhancement in 83.3%. Homogenous enhancement and clumped non-mass enhancement were seen only in two cases(8.3% each). These results conform to many studies regarding the presence of microcalcifications **[21-23]**.

Pathological microcalcifications tend be frequent among these tumors because they usually encompass DCIS **[24]**. Algazzar et al., studied Her2-neu enriched tumors on both mammography and MRI and found that these tumors tend to present with pathological microcalcifications (70% compared to 50% in our study). On MRI they are usually mass lesions with irregular margins (61.5%). Similar to our results they can present with NME (38.5% VS 25% in our study). Whether mass or NME, the enhancement pattern is often heterogenous (84.6% vs 83.3% in our study) **[22]**. Meta analysis study performed by Elias et al., found that suspicious microcalcifications were a high risk for Her2-neu enriched cancers regardless of presence of a mass lesions **[25]**.

TN cancers are more common among younger patients and those with BRCA1 mutations. They tend to be high-grade tumors and carry increased risk of metastasis and recurrence. They hold the worst prognosis among the molecular subtypes **[7]**. TN cancers are more cellular and grow rapidly compared to other subtypes. Usually, they don't induce desmoplastic reactions in the surrounding breast parenchyma. That why they tend to have rather well-defined margins **[24]**. In the current study TN tumors were high grade (2&3). They presented as a mass (100%) with irregular (70%) and circumscribed/lobulated margin (30%) and no pathological microcalcifications. On CESM, they elicited heterogenous mass enhancement (80%) and rim enhancement (20%). Boisserie-Lacroix, reported that TNT usually push rather than invade the surrounding tissues, resulting in circumscribed borders. Pathological microcalcifications are also rare with this type. Furthermore, on MRI they show rim enhancement **[26]**.

In accordance with our results, Y. Kojima, R. In, and H. Tsunofound that TN cancers usually develop as a mass (65-71% vs 100% in our study) with low incidence of architectural distortion and microcalcifications. These masses usually have microlobulated or circumscribed margins **[27]**. Another study reported that on MRI, TN tumors are usually mass lesions with rounded margins and rim enhancement. Similar to our results they found that NME is rare in this particular molecular subtype **[28]**. L. NavarroVilar et al., in their study found that TN cancers were mass lesions (94.1% vs 100% in the current study) and had smooth margins (62.5% vs 30% in the current study). Regarding enhancement their study showed 68.7% of TN cases had rim enhancement while 31% had heterogenous enhancement, compared to 20% and 80% in our study. This discrepancy could be attributed to the smallernumber of patients enrolled in our study.

T. Kazama et al., suggested that rim enhancement is caused by the relatively higher blood supply to the periphery of the tumor accompanied by central necrosis. Meta-analysis study performed by Nariya Cho et al., concluded that TN tumors are characterized by absence of microcalcifications. They also claim that although rim enhancement is a frequent feature of TN tumors, they commonly show heterogenous mass enhancement **[17,15]**.

Our study has its limitations mainly the small sample size with poor representation of some molecular subtypes, especially TN cancers. Also, we didn't take into consideration the tumor size as large size tumors may show more necrosis and have more heterogenicity upon enhancement. Finally the lesions were assessed using immunohistochemistry testing instead of full genetic sequencing, that could have yielded more accurate results.

Conclusion:

CESM has the potential to non-invasively differentiate the various molecular subtypes of breast cancer, particularly luminal cancers. Lesion margins can provide a clue for the molecular subtype. Luminal cancers are usually irregular masses with spiculated/irregular borders and heterogenous mass enhancement. Her2-neu enriched cancers often elicit microcalcifications and can show non-mass enhancement. TN cancers can be circumscribed & elicit both rim and heterogenous mass enhancement. The significance of these results requires further larger scale studies to establish CESM as a noninvasive tool for the prediction of the molecular subtypes of breast cancer.

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دور أشعة الماموجرام بالصبغة فى التفريق الغير تداخلى بين الأنواع الفرعية الجزيئية لسرطان الثدى ودرجة السرطان

يعد سرطان الثدى من أكثر الأمراض التى لها أكبر تأثير إجتماعى فى العالم فى الو قت الحالى حيث أنه على أرض الواقع،سرطان الثدى يعد الورم الأكثر شيوعاً وفتكاً بين النساء، وذلك على الرغم من حقيقة أن معدلات النجاة منه قد نمت فى العشرين عاماً الماضية بسبب الاكتشاف المبكر والعلاجات الأفضل بشكل عام.

عند تشخيص إصابة مريضة ما بسرطان الثدى، يتم إجراء فحص مرحلى لتقييم مدى وشدة السرطان من أجل تقديم أفضل رعاية ممكنة والتنبؤ بمخاطر التكرار ومعدلات حدوث الوفاة. يتم تصنيف سرطانات الثدى التى يتم الحصول على عينة منها عن طريق الخزعة أو الجراحة اعتماداً على مظهر الخلايا السرطانية تحت المجهر مقارنة بالخلايا السليمة. يتم تقييم الدرجات النسيجية على مقياس من ١ إلى ٣ حيث تشير الدرجات الأعلى إلى وجود خلايا شاذة أكثر فى الفحص المجهرى، فالدرجات النسيجية الأ على تشير إلى ورم خبيث وتو قعات سيئة

لقد أدرك علماء الأمراض منذ فترة طويلة التنوع المورفولوجى الشكلى وكيف ينعكس فى العديد من الأنواع النسيجية الفريدة لسرطان الثدى، فلكل منها شكلها المجهرى الخاص ونتائجها السريرية. يوجد أنواع فرعية جزيئية مختلفة لسرطان الثدى. كل نوع فرعى جزيئى له تشخيصه وطريقة علاجه. يعد تحديد هذا النوع الفرعى الجزيئى ضرورياً للسماح بالعلاج الفردى للمريض.

التصوير الشعاعى باستخدام أشعة الماموجرام بالصبغة هو أداة حديثة نسبياً فى تقنيات تصوير الثدى التى تجمع بين مزايا التصوير الشعاعى للثدى الرقمى كامل المجامع استخدام مادة تباين فى الوريد. ومن المميز فى التصوير الشعاعى باستخدام أشعة الماموجرام بالصبغة أنه يستفيد من تكوين الأوعية الورمى من خلال السماح لعوامل التباين بالتأكيد على مناطق الأوعية الدموية الجديدة مقارنة بأنسجة الثدى الطبيعية المحيطة.

تؤكد النتائج الحالية على أن التصوير الأشعاعى باستخدام أشعة المامجرام بالصبغة قد يكون لها ميزة فى التنبؤ بالنوع الفرعى الجزيئى فى أورام سرطان الثدى. وبهذه الطريقة يمكن أن يوفر معلومات حول الورم ككل وليس فقط الجزء المأخوذ من الورم.