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Evaluation of molecular subtypes of breast cancer using MRI BI-RADS Lexicon

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Abstract

Background Molecular subtyping of breast cancer is one of the prognostic factors which play a very important role in managing patient's treatment plan. The MRI BI-RADS Lexicon is initially used to categorize breast lesions but recent attempts were employed to differentiate breast lesions based on their molecular subtypes using this lexicon. The study aimed to evaluate of the role of the MRI BI-RADS Lexicon in classifying different molecular subtypes of breast cancer especially after coupling with Kaiser scoring system.

Methods This retrospective study was conducted on 147 patients with 170 malignant breast lesions. They underwent Pre-contrast and a Dynamic contrast MRI study. Retrospective interpretation of the morphological and dynamic criteria of the breast lesions based on the MRI BI-RADS criteria was carried out followed by reassessment of the same lesions by Kaiser scoring. Resulting data were correlated with histopathological and immunological characterization.

Results Luminal subtypes were more frequently encountered as mass lesions, contrary to the Non-Luminal lesions which showed a more frequent non-mass presentation value (P 0.002). The shape, margin, internal enhancement pattern of the mass lesions showed significant variability between different molecular subtypes ($P < 0.001, < 0.001, < 0.001$) respectively. On Dynamic study, Plateau curve was a more evident pattern with Luminal lesions contrasting with their Non-Luminal counterparts which showed a washout pattern more frequently (P 0.0004). Most of luminal A cancers were presented as mass lesions with rim enhancement and categorized as BIRADS 4 while most of Her2neu positive cancers (including luminal B entity) were presented as non-mass lesions with irregular shape and dark internal septations and categorized as BIRADS 5 with statistically significant values ($P < 0.001$). Coupling with Kaiser scoring system improved the categorization of non-luminal tumors as BIRADS 5 lesions especially the aggressive TN cancers.

Conclusions MRI-BIRADS lexicon can be of great value in the non-invasive molecular characterization of breast cancer. Kaiser score improved the categorization of TN cancers which were upgraded to BIRADS 5 category.

Keywords BIRADS lexicon, ACR BIRADS, Molecular subtypes, Breast cancer molecular subtypes

Background

The difficulty of managing breast cancer is well known. Prognosis and treatment are currently determined largely on the basis of breast cancer stage however in the modern era it is guided by sophisticated molecular tools to help select and guide therapy [1].

The molecular classification of breast cancers defines subgroups of cancer with different prognoses and treatments. Each molecular type representing the intrinsic signature of the cancer corresponds to a histological profile incorporating hormone receptors, HER2 status and

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the proliferation index. The four Molecular types include Luminal A, Luminal B, HER2neu enriched and Triple negative [2].

Having a standard, customized radiological reporting system of imaging findings (BI-RADS) will offer better cooperation for the sake of the patient [3]. In 1993, with the goal to standardize the mammography reports, the Lexicon was created. So, the BI-RADS Lexicon is mainly created to eliminate vagueness in reporting and so facilitating the communication between radiologists and physicians. Structured reports include several categories including, breast density, description of features and finally the BIRADS score. In 1995, 1998, there was addition of the atlas with examples to each descriptor. In 2003, US and MRI imaging standardization, then in 2014, the much-anticipated fifth edition of the American College of Radiology (ACR) (BI-RADS) lexicon was released. So, using the lexicon makes sure that there is a quality control for the radiology reports [4].

Previous studies on the MRI BI-RADS and its correlation with phenotypes of breast cancer have serious limitations being retrospective [5]. Moreover, they included independent features of the system rather than the final score of the BIRADS Lexicon. So new simple, abbreviated and easily implemented scoring systems were tried for assessment of breast cancer subtyping such as Kaiser score flow chart [6].

Methods

Study design and patients

This retrospective study was approved by the Institutional review board. The study included 170 breast lesions with pathologically proven breast cancer of different molecular subtypes. Each had a systemic imaging analysis based on the MRI-BIRADS Lexicon. Imaging characteristics were correlated to each phenotype.

MRI technique

Magnetic resonance imaging examinations were performed with the patients in the prone position by using a 1.5-T MRI unit (Gyroscan Intera; Philips Medical Systems, Best, the Netherlands) with breast surface coils. A localizing sequence was followed by axial turbo spin-echo T2-weighted imaging (repetition time ms/echo time ms, 4684/130; matrix, 256×256). Other parameters were as follows: field of view (FOV), 35 cm; section thickness, 4 mm; and intersection gap, 0 mm.

After, DWI Spin-echo was performed using spectral attenuated inversion recovery (SPAIR) sequence on the axial plane with the following parameters: TR/TE 9373/72 ms, matrix 80 9 80 pixels, FOV 34 cm, slice thickness 4 mm and acquisition time 224 s and two order factor b (0 and 800).

This examination was followed by a dynamic study that consisted of serial imaging by axial with a three-dimensional fast field-echo T1-weighted sequence (4.0/ 2.0; flip angle, 10°; matrix, 352 9 352) with fat suppression (SPAIR). The parameters were as follows: FOV, 44 cm; section thickness, 2 mm; and intersection gap, 0.8 mm. Gadodiamida (Omniscan; General Electric Healthcare, Bio-Sciences, La Florida, Madrid, Spain) was administered as a bolus intravenous injection (2 mL/s) at a dose of 0.1 mmol/kg of body weight followed by a 20 mL saline solution flush.

Other acquisition fast field-echo T1-weighted sequence by sagittal acquisition and with fat suppression (SPAIR) was performed over a period of 6 min after intravenous contrast material injection, the parameters were as follows: 4.0/2.0; flip angle, 10°; matrix, 192 9 192; FOV, 44 cm; section thickness, 2.5 mm; and intersection gap, 0.8 mm. Subtracted images from DCE MRI (early post-contrast- precontrast) were superimposed for cancer lesions detection.

MRI image analysis

The lesion type, according to BI-RADS was categorized into mass or non- mass like enhancement. In the mass lesions, we analyzed the shape, margin and type of enhancement, while in the non-mass like enhancement we examined the distribution and internal enhancement pattern. Assessment of the time-signal intensity curve, according to the BI-RADS, were categorized into three types (persistent, plateau or washout pattern).

Kaiser scoring flow chart

Is a clinically based simple algorithm used to provide simple assessment tool of breast lesions followed by providing suitable recommendations for the clinicians according to final lesion scoring. It consists of a classification tree of the five most powerful diagnostic criteria the BIRADS lexicon (including speculations, MRI enhancement curves, margins, internal enhancement pattern and edema). A scoring system is reached by using the Kaiser flowchart: low risk breast lesion has a score of [1–4], intermediate risk lesions [5–8] and high risk lesions [8–11]. The main value of this scoring system is its simplicity in evaluation of breast lesions especially when used by less experienced radiologists. This scoring system was applied to all lesions and compared to BIRADS lexicon to detect the degree of interobserver agreement between them, using a secondary work station (Phillips Advantage Windows workstation with functional tool software), MR images were analyzed retrospectively by 2 radiologists (D.B. and F.S.) who have experience in breast imaging for 15 and 8 years, respectively. The first radiologist analyzed

Table 1 Mass/NME in relation to molecular subtype and their dynamic curve assessment:

	Luminal (*N* = 130)	Non-luminal (*N* = 40)	*P*
Mass/non-mass lesions			
Mass lesions	108 (83.1%)	22 (55.0%)	0.002*
Non-mass lesions	22 (16.9%)	18 (45.0%)	
Dynamic enhancing curve			
Plateau (type II curve)	52 (40%)	4 (10%)	0.0004*
Washout (type III curve)	78 (60%)	36 (90%)	

Data expression: *N* (%). *P* value: Chi-Square and Fisher's exact test

* demarcates the statistically significant results

the lesions using BIRADS lexicon, then the second radiologist reanalyzed the same lesions that was identified by the first radiologist using Kaiser flow chart separately.

Statistical analysis

To compare the MRI findings, mass or non-mass like enhancement, between the subtypes of breast cancer, we used the chi-square test or the Fisher exact test.

All analyzes were performed by using software (SPSS version 15.0; SPSS, Chicago, IL), with $p < 0.05$ considered to indicate a significant difference.

The weighted κ statistic including 95% confidence interval (CI) with percentage agreement was done to estimate the proportion of agreement of our radiologists for lesion assessment by BIRADS lexicon and Kaiser Score. The κ values were interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.

Results

Luminal subtypes showed a more frequent mass presentation contrary to non-luminal subtypes which is more frequently represented as non-mass lesions ($P = 0.002$). We analyzed the mass lesions separately ($N = 130$), Table 2. Mass lesions were analyzed based on their margin, their shape, and the internal enhancement patterns. Chi-square and Fisher exact tests showed the relationship between different mass morphological criteria and their molecular subtypes. None of the (Her + ve) lesions had a smooth margin however, most of them had a spiculated margin (P value of < 0.001). While all Triple negative mass lesions had a smooth margin (P value of < 0.001). None of the Non luminal lesions had an irregular margin while none of the Luminal lesions had smooth margin.

In terms of hormonal status none of the ER (+ ve) or PR (+ ve) lesions had a round or oval shape, while the majority of the ER + v, PR + ve lesions and Her2 -ve lesions had irregular shape. None of the luminal B lesions were round, and none of the TN caners were irregular. These findings were statistically significant, with a P value of 0.001.

Table 2 Morphological features of mass lesions in differentiation of molecular subtypes of breast cancer using the MRI BIRADS lexicon (N = 130)

	Luminal A (*n* = 16)	Luminal B (*n* = 92)	Triple negative (*n* = 14)	Her2neu (*n* = 8)	*P* value
Shape					
Round/Ovalr	0 (0.0%)	0 (0.0%)	14 (100.0%)	2 (25.0%)	< 0.001*
Irregula	16 (100.0%)	92 (100.0%)	0 (0.0%)	6 (75.0%)	
Margin					
Irregular	14 (87.5%)	6 (6.5%)	0 (0.0%)	0 (0.0%)	< 0.001*
Spiculated	2 (12.5%)	86 (93.4%)	2 (14.3%)	8 (100.0%)	
Smooth	0 (0.0%)	0 (0.0%)	12 (85.5%)	0 (0.0%)	
Enhancement pattern					
Heterogeneous	6 (37.5%)	40 (43.4%)	2 (14.2%)	6 (75.0%)	< 0.001*
Rim	8 (50.0%)	12 (13.04%)	8 (85.7%)	0 (0.0%)	
Dark internal septations	2 (12.5%)	40 (43.4%)	0 (0.0%)	2 (25.0%)	

Data expression: *N* (%). *P* value: Chi-Square and Fisher's exact test

* demarcates the statistically significant results

Table 3 Kaiser Score and BIRADs lexicon final category of the lesions in differentiation between molecular subtypes, receptor status and histological subtypes

	Luminal A (*N* = 22)	Luminal B (*N* = 108)	Her2neu (*N* = 22)	TN (*N* = 18)	*P* value	ER/PR + ve (*N* = 130)	ER/PR -ve (*N* = 40)	*P* value	Ki 67 < 14% (*N* = 50)	Ki67 ≥ 14% (*N* = 120)	*P* value
BIRADs Lexicon											
BIRADS 4	18 (81.8%)	24 (22.2%)	10 (45.5%)	14 (77.8%)	0.001*	42 (32.3%)	24 (60%)	0.001*	26 (52.0%)	26 (21.7%)	0.0009*
BIRADS 5	4 (18.2%)	84 (77.8%)	12 (54.6%)	4 (22.2%)		88 (67.7%)	16 (40%)		24 (48.0%)	94 (78.3%)	
Kaiser score category											
BIRADS 4	18 (81.8%)	30 (27.8%)	2 (9.1%)	0	< 0.001*	48 (36.9%)	2 (5%)	0.010*	22 (44.0%)	14 (11.7%)	0.001*
BIRADS 5	4 (18.2%)	78 (72.2%)	20 (90.9%)	18 (100%)		82 (63.1%)	38 (95%)		28 (56.0%)	106 (88.3%)	

Data expression: *N* (%). *P* value: Chi-Square and Fisher's exact test

* demarcates the statistically significant results

Table 4 Agreement on BIRADS categorization using the BIRADS score and the Kaiser score

Cohen's κ	95% CI	*P* value	Agreement		Disagreement	
			B4	B5	B4/K5	B5/K4
0.534	0.403–0.664	0.001	40	94	26	10

κ Kappa. *CI* Confidence interval. *B* BIRADS final category using the BIRADS lexicon, *K* BIRADS final category using the Kaiser score

Regarding the Non-Mass lesions ($N=40$) abnormal non mass enhancement pattern in our study were either clumped or heterogeneous. ER (+ve) status, PR (+ve) status and Her2neu (− ve) status were more represented by clumped non-mass enhancement. While ER (− ve) status, PR (− ve) status, Her2neu (+ve) status and TN were more likely to be represented by heterogeneous pattern of enhancement with no detected statistical significance.

The Time intensity curve (TIC) analysis showed that 40% of the luminal lesions showed plateau curve and had an ER (+ve) and PR (+ve) status, while 90% of the non-luminal lesions showed wash out curve and had an ER (− ve) and PR (− ve) status, and a statistically significant *P* values of (*P* value of 0.0004) as shown in Tables 1 and 2.

By Kaiser scoring flow chart, the majority of the lesions (96%) with intermediate risk of breast cancer showed an ER(+ve) status, PR (+ve) status, with significant *P* values of (0.010), (0.001) respectively. Out of the non-luminal lesions 38 (95%) of them showed high risk of breast cancer and had ER (− ve) status, PR (− ve) status. All TN lesions were of high risk (scoring 8–11). This was statistically significant with a *P* value of (< 0.001). In our study, the specificity of the Kaiser Flow tree to exclude triple negative in absence of BIRADS 5 category was (100%) as shown in Table 3.

A statistically significant *P* value was obtained when using the final BIRADS category to sort lesions according to their molecular subtypes (*P* value < 0.001) by the Kaiser Flow tree. Also, it successfully differentiated Luminal A from Luminal B lesions where luminal B lesions were more frequently represented by BIRADS 5 category and the opposite is true for Luminal A which were more frequently represented by BIRADS 4 category.

A statistically significant moderate interobserver agreement on final BIRADS assessment of the lesions using the BIRADS lexicon and the Kaiser score (*P* value 0.001) as shown in Table 4. This implies that Kaiser Score uses 5 powerful descriptors that can reach the final BIRADS category omitting lots of redundant descriptors used by the BIRADS lexicon (Figs. 1, 2, 3, 4, 5, 6, 7 and 8).

Discussion

In this study, lesions were classified into either mass or non-mass enhancement. Our study included 170 lesions, 130/170 of the lesions were mass lesions and 40/170 of them were non-mass lesions. Of the 130 mass lesions, the molecular subtype of 108 of them was luminal (16/108 of them were luminal A and 92/108 of them were luminal B) and the molecular subtype of 22/130 of them were non-luminal (8/22 were Her2neu and 14/22 were TN subtype). NME was represented by 40 lesions (22/40 were luminal, and 18/40 were non-luminal with (14/18 her2neu subtype and 4/18 TN subtype).

Luminal subtype was more frequently presented as mass lesions. While non-luminal lesions or an ER/PR -ve status as more seen as NME. This was a statistically significant with a *P* value of ($P=0.002$). TN breast cancers were also more frequently represented as mass lesions while Her2neu lesions showed NME more frequently. These results were like those concluded by Vilar et al. [7]. In general, a positive hormonal status was more frequently related to mass lesions.

The morphological criteria of the mass lesions including margin, shape and internal enhancement patterns were studied. Regarding the margins of the mass lesions, all lesions with irregular margins and spiculated margin lesions were of luminal subtype. Margin of Luminal A subtype lesions were more frequently irregular (87.5%) while margin of Luminal B lesions was more frequently spiculated (93.4%), this was statistically significant with a (*P* Value < 0.001). These results were in line with the study conducted by Vilar et al. [7]. Also, there was a statistically significant correlation between a spiculated margin and HER2 subtype this was in agreement to Vilar et al. [7] and Trop et al. [8]. Also, a statistically significant correlation between smooth margin and TN status was noticed. These findings showed a significant (*P* value of < 0.001). Our findings were in line with Grimm et al. [9], Yonk et al. [10], and Sung et al. [11] who reported a higher frequency for smooth border to TN masses. Boisserie-Lacroix reported that familial cancers tend to exhibit

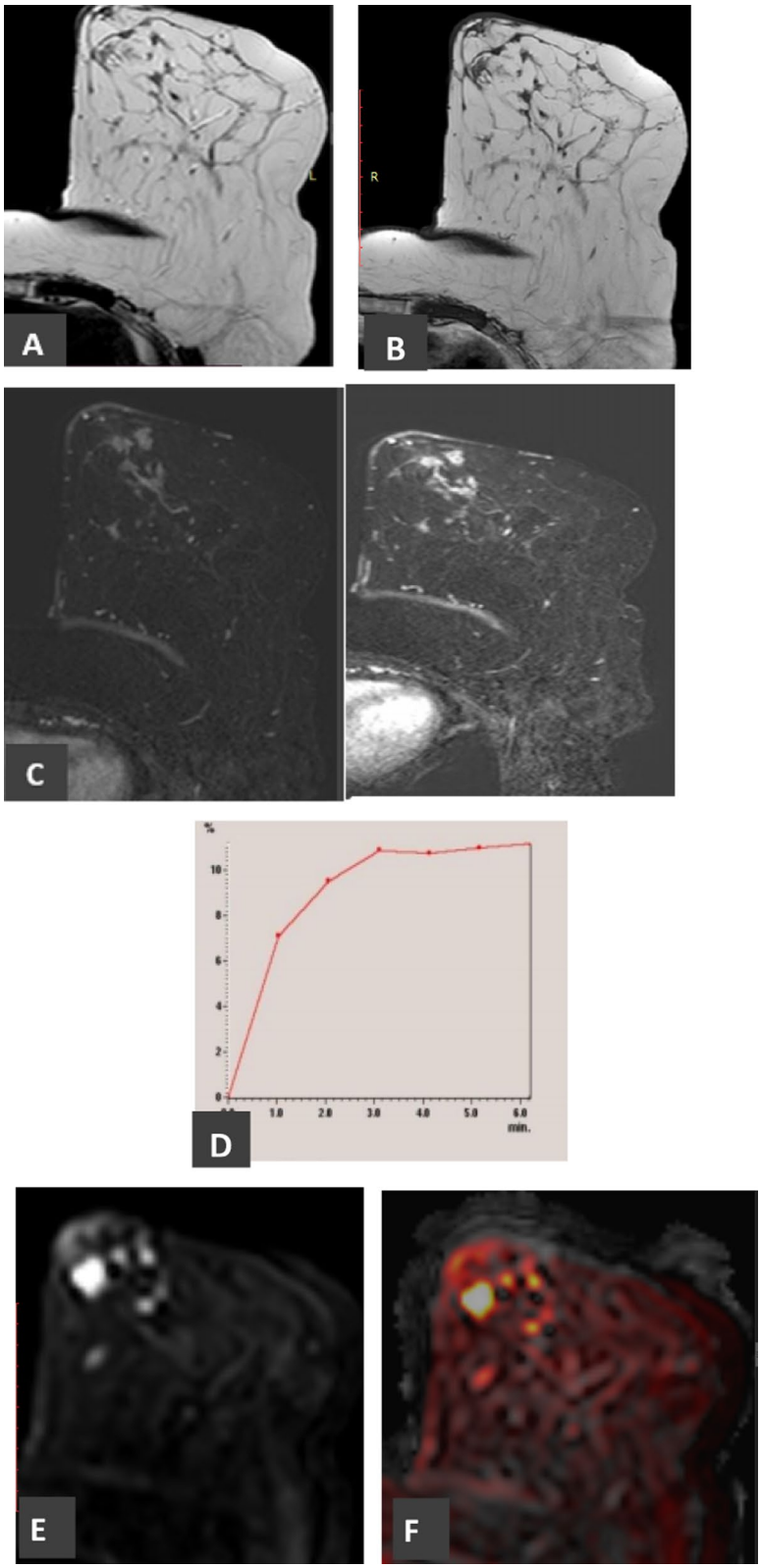


Fig. 1 **A** T1-WI showing multiple regions of low signal intensity. **B** T2-WI: showing multiple regions of low signal intensity. **C** Dynamic post contrast subtraction MRI: shows multiple regions of non-mass enhancement. **D** TIC: exhibiting type II (plateau enhancement) curve. **E** DWI at b = 1000: the lesion shows high signal intensity. **F** Axial grayscale ADC map: showing the lesion with restricted diffusion and calculated Mean ADC value: 0.5. *Final molecular diagnosis: Luminal A breast cancer. BIRADS (MRI-Lexicon):4, BIRADs (Kaiser Score): 5*

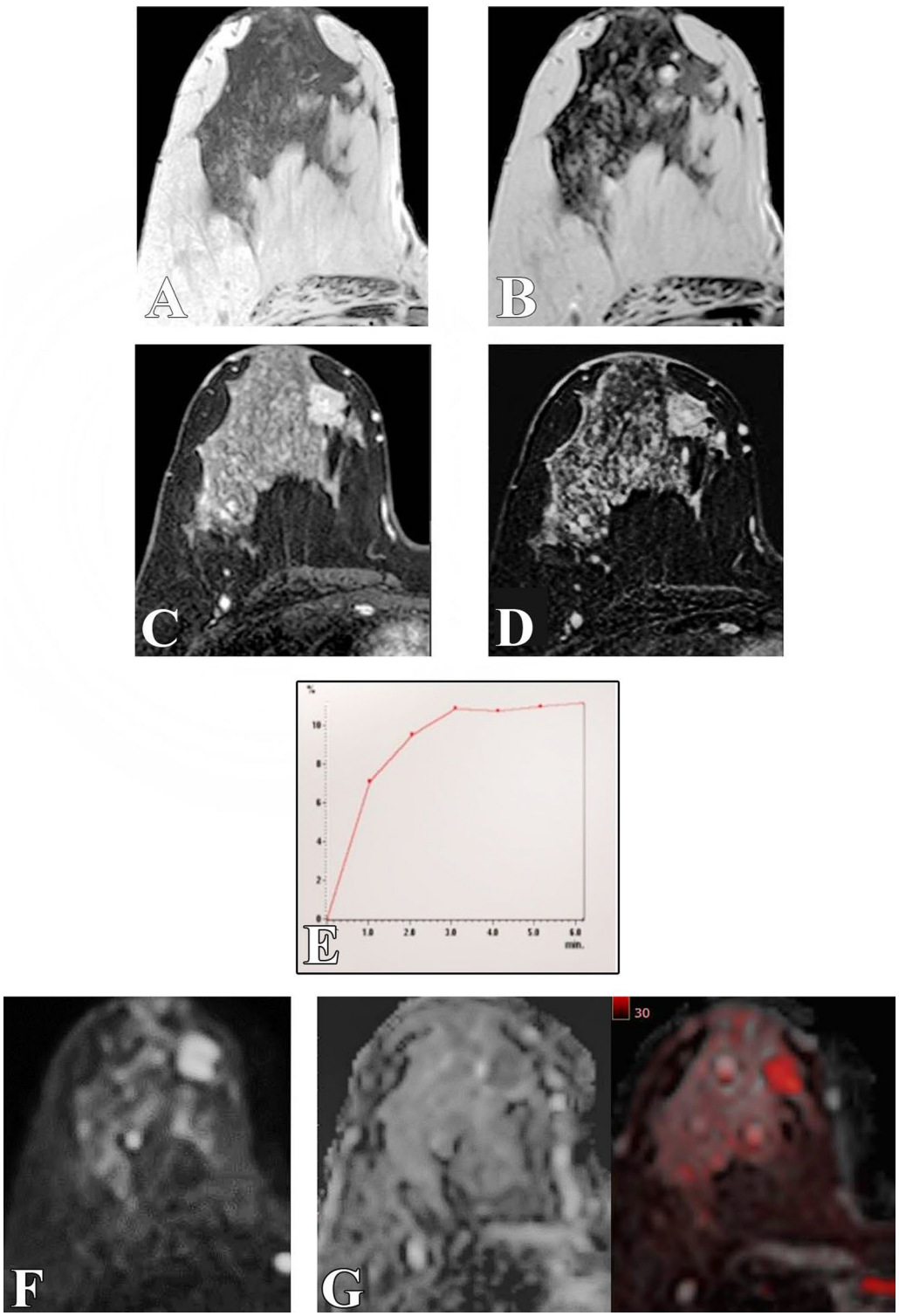


Fig. 2 **A** T1-WI: showing an ill-defined area of the intermediate signal intensity at the LOQ. **B** T2-WI: a non -circumscribed mass of irregular shape and margin is seen at the previously described area on T1WI at the lower inner quadrant of the right breast. It exhibits intermediate high SI. **C**, **D** Dynamic and subtraction images: The irregular shape and margin of the previously described mass are now more evident. The mass shows a heterogeneous enhancement pattern. **E** TIC: exhibiting type II (plateau enhancement) curve. **F** DWI at b = 1000: the lesion shows high signal intensity. **G** Axial grayscale ADC map: showing the lesion with restricted diffusion and calculated mean ADC value = 0.6 X10 – 3 mm2 /s. *Final molecular diagnosis: Luminal A breast cancer. BIRADS (MRI-Lexicon):4, BIRADS (Kaiser Score): 4*

smooth mass margins. Accordingly, specific subtypes of high-grade tumors, such as triple-negative and familial breast cancers are likely to manifest with benign morphologic criteria [12].

Other studies discussed that irregular margin is more frequent than smooth margin regarding TN mass lesions [13]. Others as Shin et al. [14] stated that spiculated margin is more related to hormonal negative status. Our explanation to this controversy is that we studied the Her2 hormonal status besides the ER and the PR which was not carried out by Shin et al. [14]. Also, studies before 2013 referred to the 4th BIRADS lexicon and not the 5th which had changed regarding describing the margins of the mass. Observation of literature shows that there is slight inter-observer variability when applying the BIRADS descriptors.

In this study, there was an association between shape of the mass and non-luminal subtypes where triple negative subtype mass lesions were more frequently round. Irregular shape was detected more in luminal lesions. This was statistically significant with a (P value of < 0.001).This was in agreement with Vilar et al., Grimm et al. and Sung et al. [7, 9, 11]. However, it was in contrast to Chen et al. [15] who stated that Luminal and Her2neu mass lesions were more frequently related to the round shape than Triple negative subtypes.

Finally, there was an association between internal enhancement pattern and non-luminal mass lesions (with statistically significant P value $= 0.001$), where triple negative mass lesions are more often represented by rim enhancement than heterogeneous enhancement or dark internal septations (in terms of frequency 8/14 (85.7%) TN cancers showed rim enhancement). However, the most frequent pattern representing Her2neu lesions was the heterogeneous pattern 6/8 (75%). On the other hand, dark internal septations pattern more frequently represented the luminal subtypes (predominantly Luminal B 40/92, 43.4%). Regarding the dominance of rim enhancement in triple negative lesions, Vilar et al., Moffa et al. and Trop et al. reached the same conclusion [7, 16, 17]. As for Her2neu mass lesions, there was no dominant pattern of enhancement related to it in the study conducted by Vilar et al. [7] however, similar to our study heterogeneous pattern was dominant in the study conducted by Trop et al. [8].

Lesions with non-mass enhancement were evaluated regarding their distribution and enhancement patterns. There was no significant influence of the molecular subtypes on the distribution of the non-mass enhancement criteria or distribution. Abnormal non mass enhancement pattern in our study were either clumped or heterogeneous. ER (+ve) status, PR (+ve) status and Her2neu (− ve) status were more represented by clumped non-mass enhancement. While ER (− ve) status, PR (− ve) status and Her2neu (+ve) status were more likely to be represented by heterogeneous pattern of enhancement and this was in agreement with Vilar et al. [7].

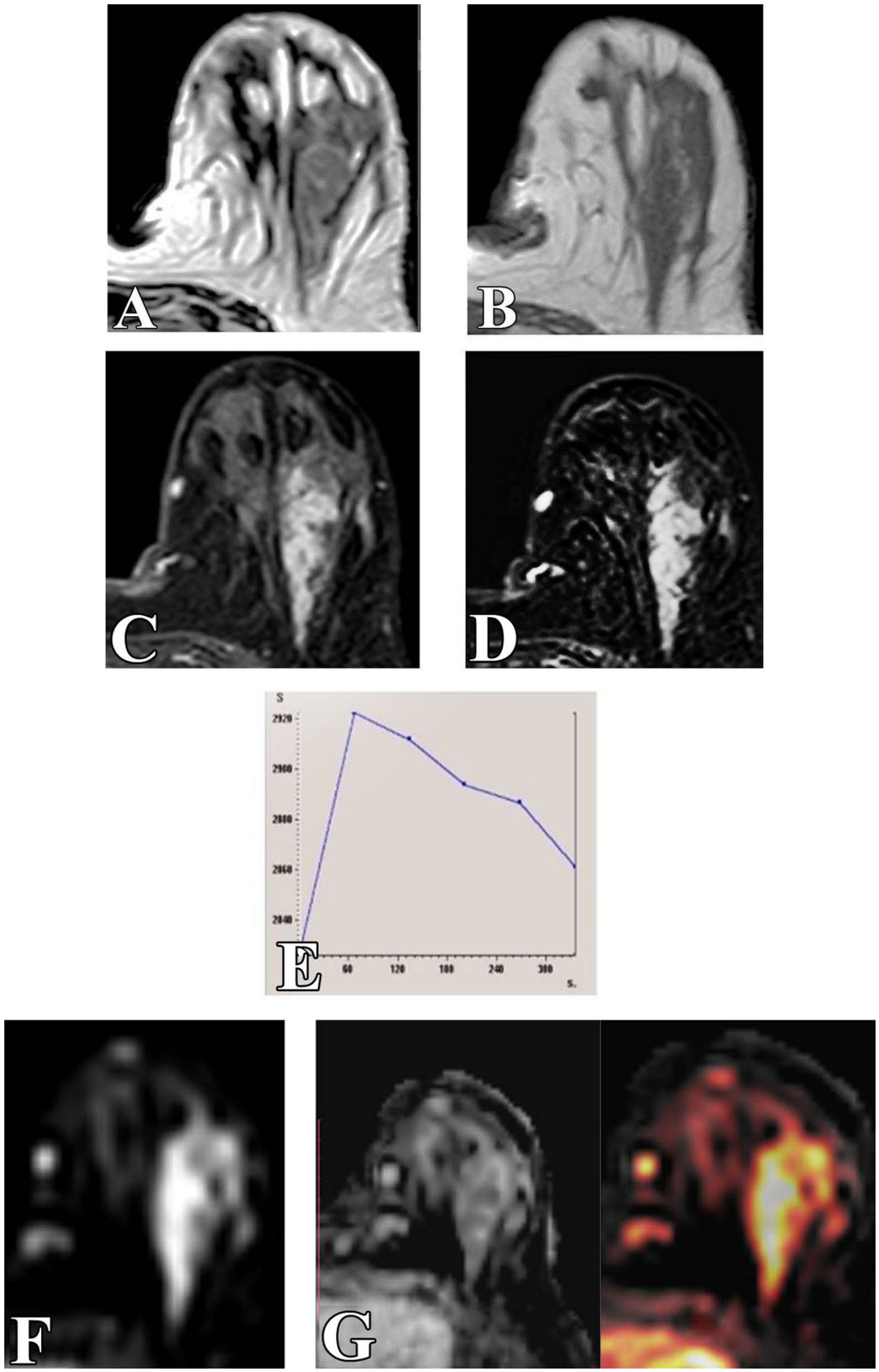
Regarding the Time intensity curve (TIC), the washout kinetics were more correlated with the non-luminal subtypes with ER (− ve) and PR (− ve) status rather than the luminal subtypes with ER (+ve) and PR (+ve) status this was statistically significant with (P values of 0.0004). Our results were also in line with the results stated by Johnson et al. [18], while Dogan et al. [19] and Galati et al., [20] stated that non-luminal lesions especially those presented by non-mass enhancement and TN cancers more frequently showed plateau curves.

As previously discussed, although the BIRADS Lexicon has been agreed to be the standard vocabulary for describing any breast lesion, it has a major limitation that lots of descriptors are addressed to reach a BIRADS category, some of clear significance and others are of less significance. Add to that, that it must be interpreted by an experienced radiologist. Some studies in literature even agreed that there is slight inter-observer agreement ($\kappa = 0.11$) when giving the final BIRADS category as this study conducted by Grimm et al. [9].

For these reasons Kaiser used five of the most powerful diagnostic criteria omitting redundant information in classification tree. The Kaiser score was also applied to all lesions and studied in relation to the molecular subtypes of the lesions, by using the tree flowchart, a score is reached which determines the possible risk of cancer. In our study high risk cancers were luminal B, TN and Her2neu matching literature that these are more aggressive than Luminal A cancers. After interpreting the Kaiser score into their BIRADS counterparts, it was able to place TN breast cancers in the BIRADS 5 category which eliminates the false sensation of benignity some

(See figure on next page.)

Fig. 3 **A** and **B** T1-WI and T2WI: a non-circumscribed area of intermediate signal intensity at the upper half of the left breast. **C** and **D** Dynamic and subtraction post contrast MRI: an area of abnormal non-mass enhancement at the upper half of the left breast. It has a segmental distribution and heterogeneous pattern of enhancement. **E** TIC: shows type III (washout enhancement) curve. **F** DWI at b = 1000: the lesion shows high signal intensity. **G** Axial grayscale ADC map: showing the lesion with restricted diffusion and calculated: Mean ADC value: 0.6 X10 − 3 mm2. *Final molecular diagnosis: Triple negative breast cancer. BIRADS(MRI-Lexicon):5, BIRADS(Kaiser Score): 5*



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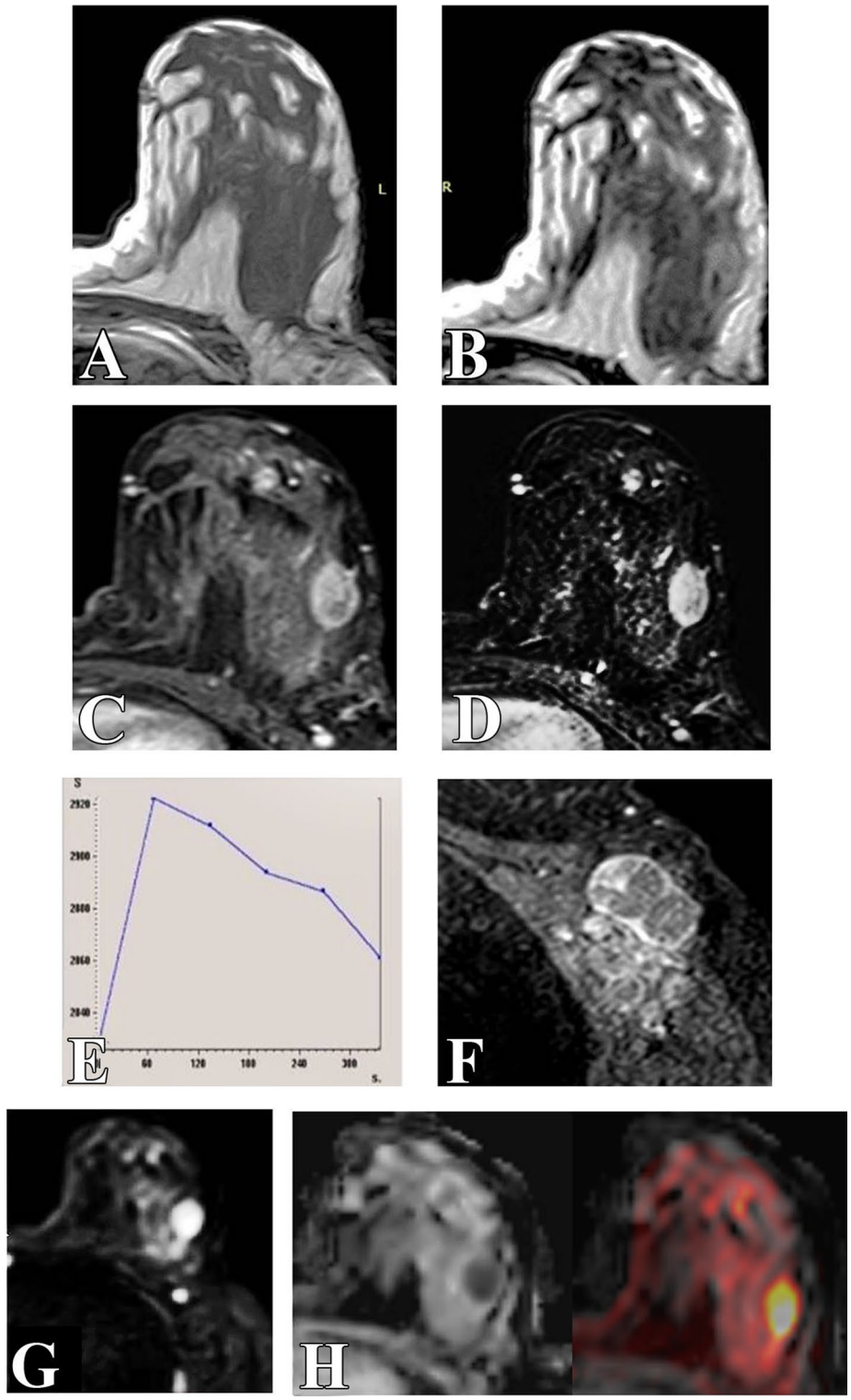

Fig. 4 **A** and **B** T1-WI and T2WI: an ill-defined area of intermediate signal intensity at the UOQ. **C** and **D** Dynamic and subtraction post contrast MRI: that shows circumscribed rounded shape mass with smooth outline. It shows rim enhancement. **E** TIC: shows type III (washout enhancement) curve. **F** Axillary LNs. **G** DWI at b = 1000: the lesion shows high signal intensity. **H** Axial grayscale ADC map: showing the lesion with restricted diffusion and calculated. Mean ADC value:0.6 X10 − 3 mm2 /s. *Final molecular diagnosis: Triple negative breast cancer. BIRADS (MRI-Lexicon):5, BIRADS (Kaiser Score): 5*

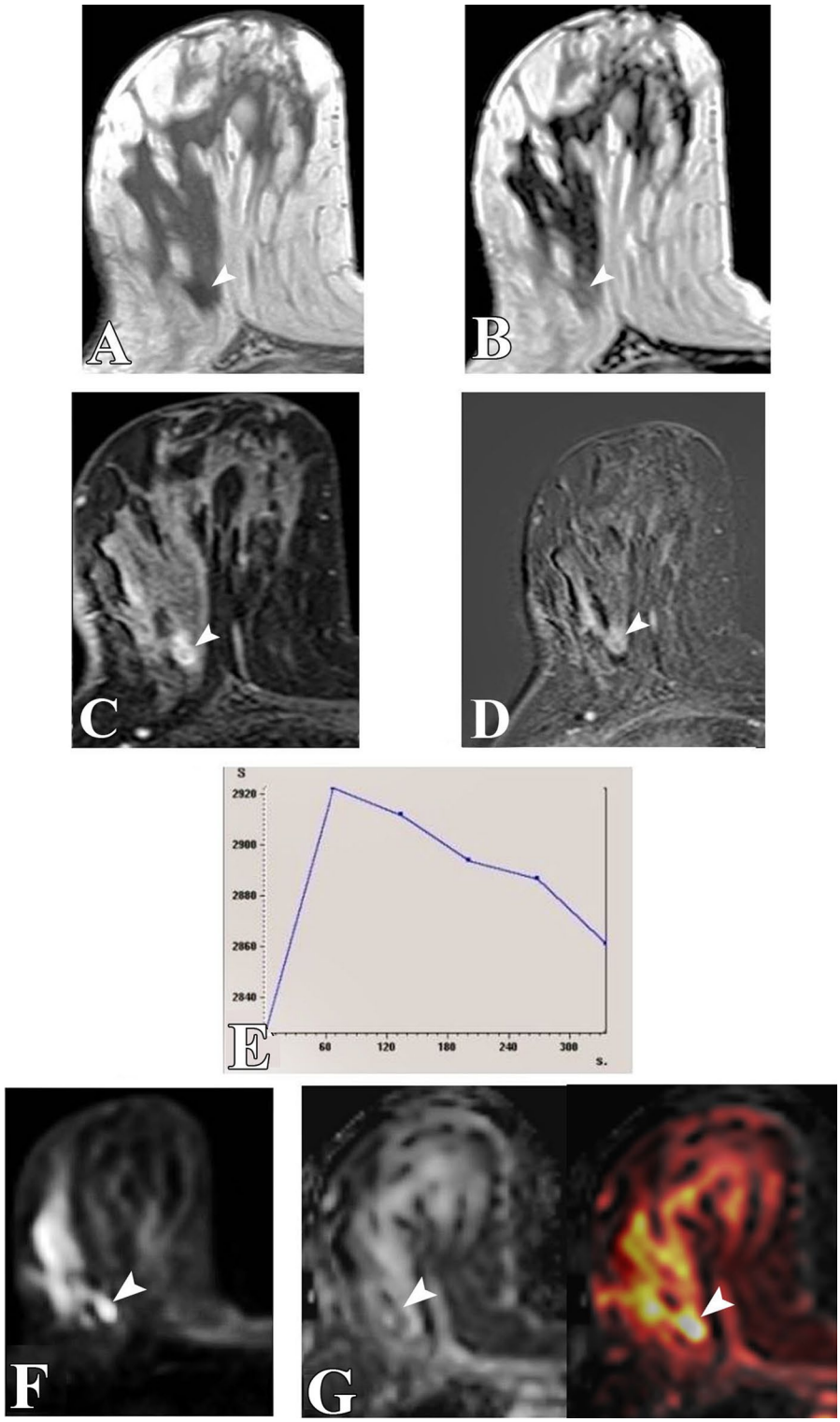

Fig. 5 **A** T1-WI: an ill-defined small area of the low signal intensity at the UOQ **B** T2WI: a small non-circumscribed rounded mass with smooth margins is seen at the previously described area of the UOQ. It shows relatively high signal intensity. **C** and **D** Dynamic and subtraction post contrast MRI: the smooth margin of the mass and its rounded shape are now more evident. The small mass shows an abnormal rim enhancement. **E** TIC: the lesion shows type III TIC (washout). **F** DWI (at b = 1000): the mass shows high signal intensity. **G** Grayscale ADC map: showing the mass with restricted diffusion and calculated mean ADC values of:0.7 X10 – 3 mm2 /s. *Final molecular diagnosis: Triple negative breast cancer. BIRADS (MRI-Lexicon):5, BIRADS (Kaiser Score): 5*

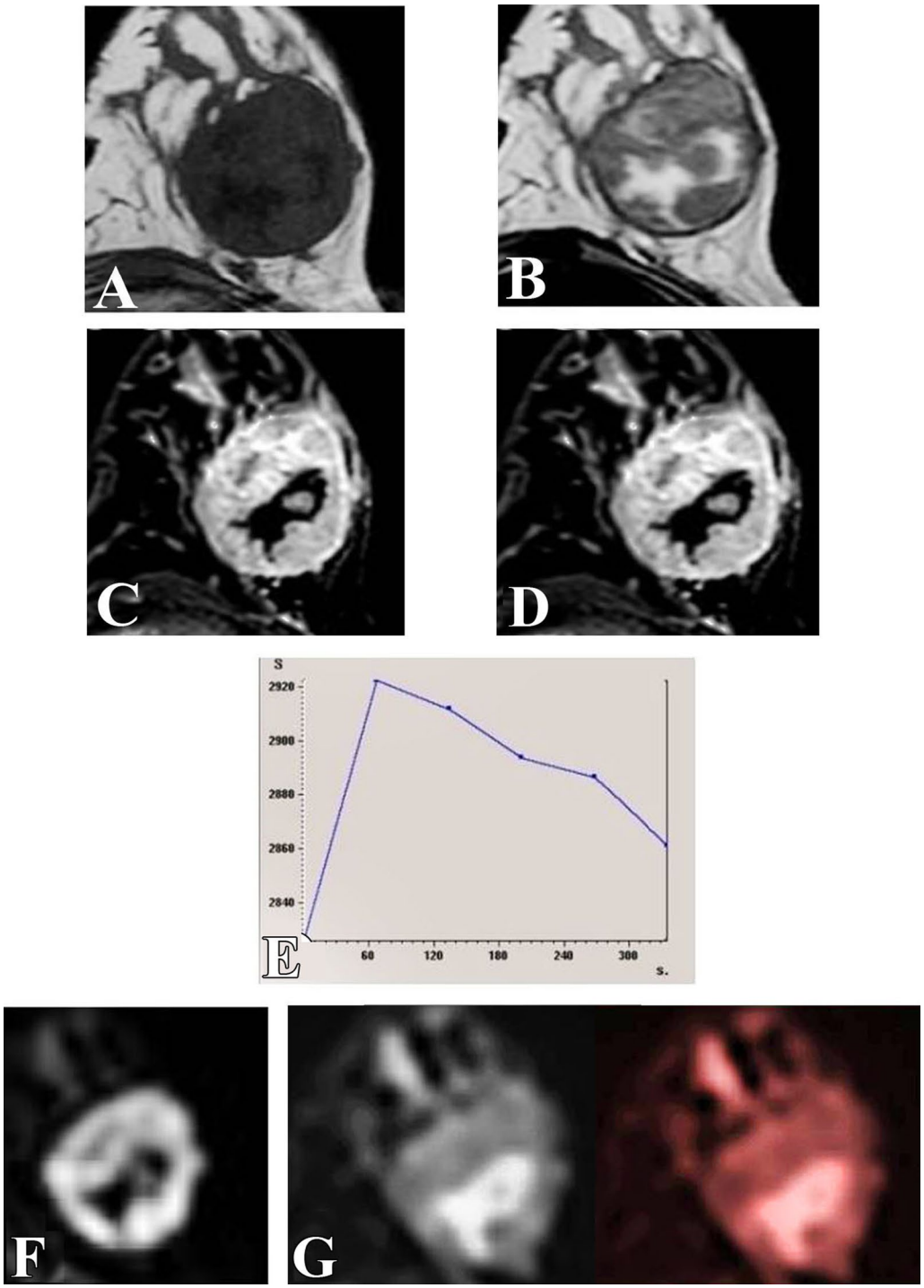

Fig. 6 **A** T1-WI: a well circumscribed rounded shape mass with smooth margins at the UOQ of low signal intensity. **B** T2-WI: the mass shows intermediate signal intensity (SI) with a central high intra-tumor signal intensity. **C** and **D** Dynamic and subtraction post contrast MRI: the smooth margin and the rounded shape are more evident. The mass shows thick rim enhancement. **E** TIC: the mass shows type III TIC (washout). **F** DWI (at b = 1000): the lesion shows peripheral high signal intensity and low central signal intensity. **G** Grayscale ADC map: the lesion shows restricted diffusion and calculated ADC mean values: 0.8 X10 – 3 mm2 /s. *Final molecular diagnosis: Triple negative breast cancer. BIRADS (MRI-Lexicon):4, BIRADS (Kaiser Score): 5*

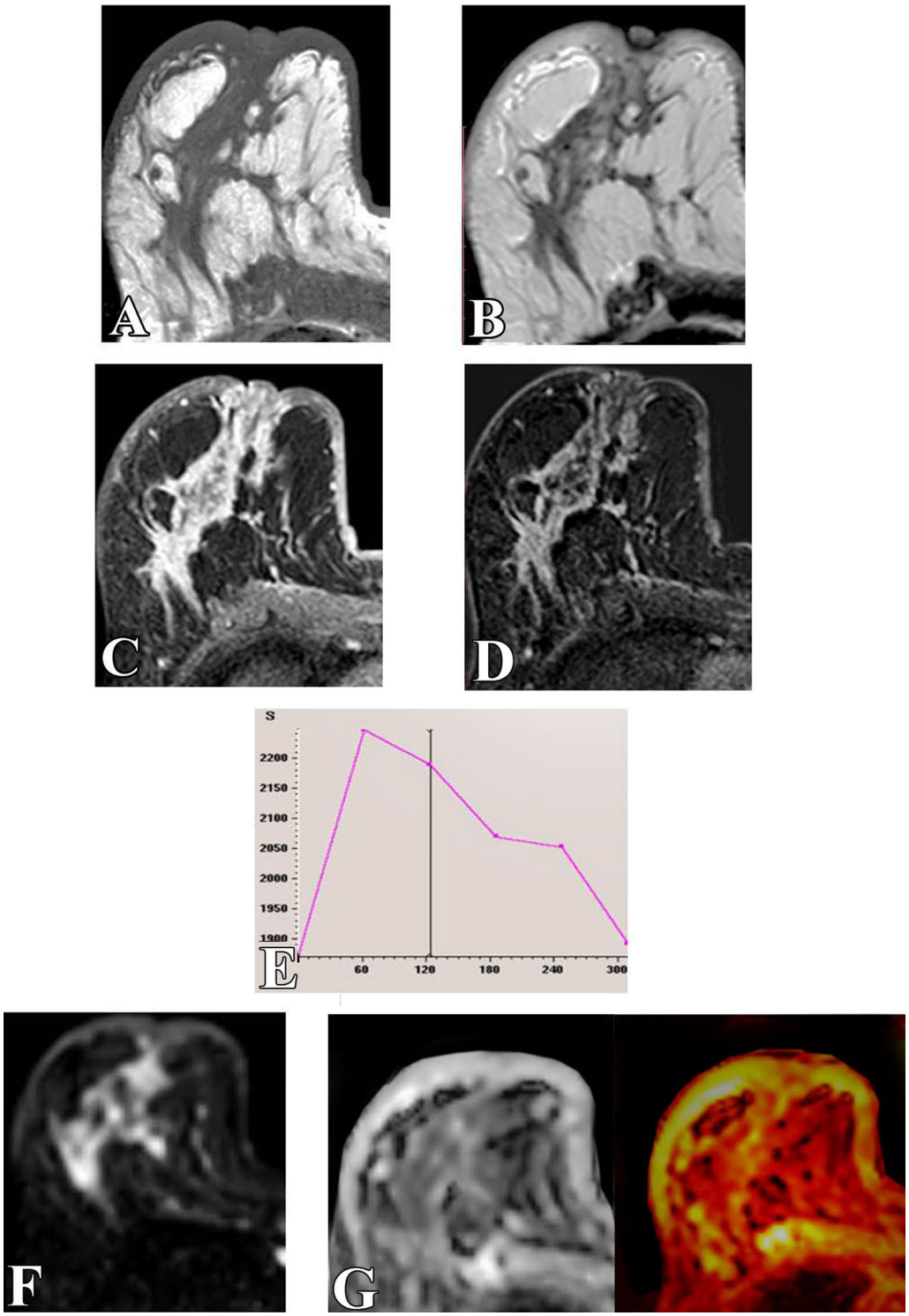

Fig. 7 **A** T1-WI: a large retroareolar area of abnormal intermediate signal intensity reaching the nipple. **B** T2-WI: this area shows relatively high signal intensity associated with subcutaneous and perilesional streaks of high SI denoting edema. **C** and **D** Dynamic and subtraction post contrast MRI: the area is seen as an abnormal non-mass enhancement reaching the nipple and skin demonstrating heterogeneous pattern and segmental distribution. **E** TIC: exhibiting type III washout curve. **F** DWI at b = 1000: the lesion shows high signal intensity. **G** Axial grayscale ADC map: showing the lesion with restricted diffusion and mean ADC value: 0.8 X10 – 3 mm2 /s. *Final molecular diagnosis: Her2neu subtype. BIRADS (MRI-Lexicon):4, BIRADS (Kaiser Score): 5*

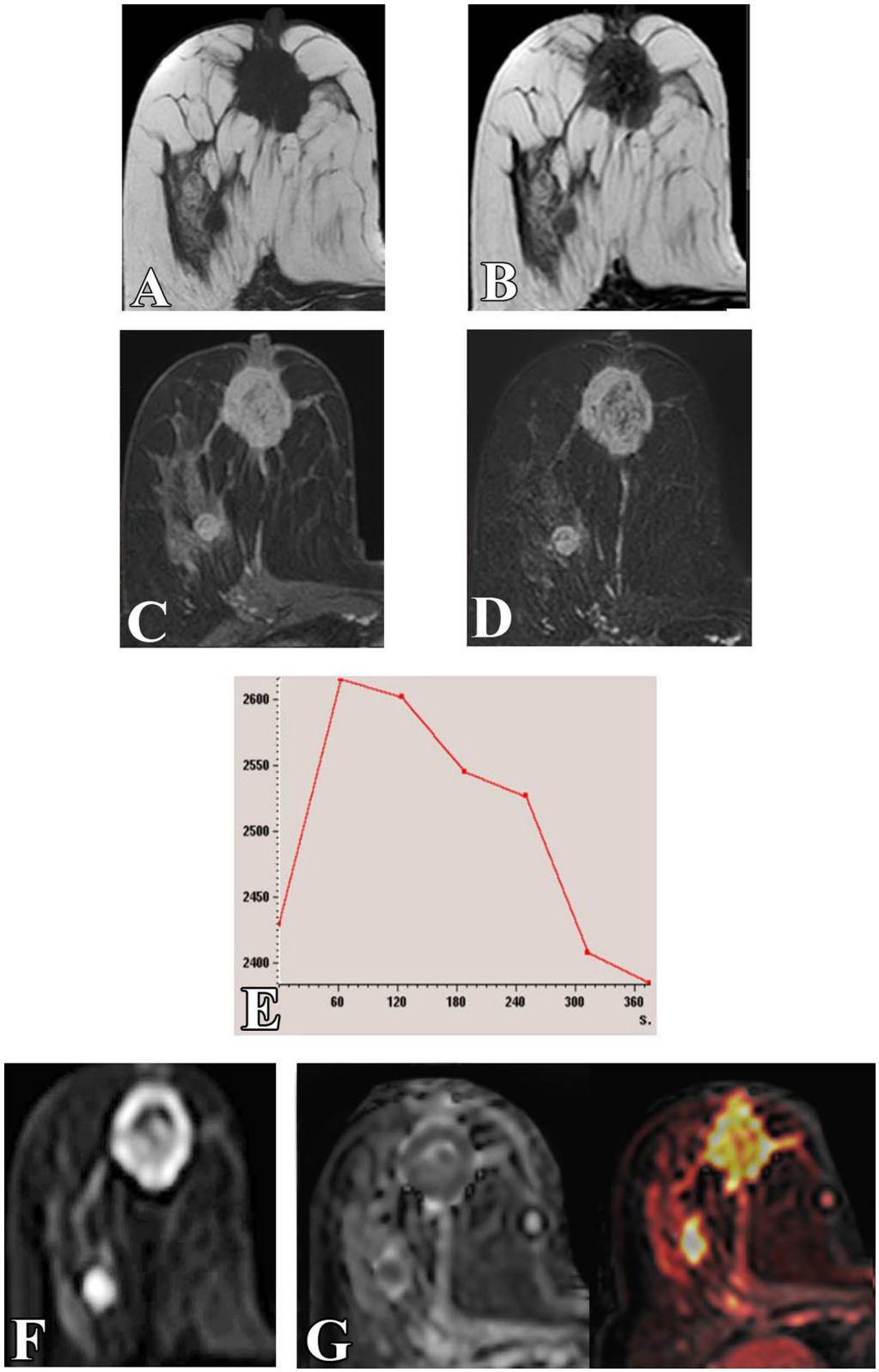

Fig. 8 (See legend on previous page.)

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Fig. 8 **A** and **B** T1WI and T2WI: showing multiple oval shaped lesions with spiculated margin. All of them show intermediate signal intensity. The largest is seen at the retroareolar region. **C** and **D** Dynamic and subtraction post contrast MRI: They all show dark internal septations pattern of enhancement. **E** TIC: shows type III (washout) curve. **F** DWI at b = 1000: all masses show high signal intensity. **G** Axial grayscale ADC map: all masses with restricted diffusion and calculated mean ADC value: 0.8 X10 − 3 mm2 /s. *Final molecular diagnosis: Luminal B subtype. BIRADS (MRI-Lexicon):5, BIRADS (Kaiser Score): 5*

TN lesions may give due to their smooth outline. This was statistically significant in differentiating molecular subtypes of breast cancer by a P value of < 0.001. A significant P value of 0.010 was also obtained in sorting ER/PR + ve from ER/PR-ve lesions. Kaiser score could also sort lesions with high Ki67 from those with low Ki67, this was statistically significant by a P value = 0.001.

A moderate agreement ($k = 0.534$) between the final BIRADS category obtained by using the BIRADS Lexicon and that acquired by applying the Kaiser score. However, further studies are required to investigate agreement between Kaiser Score and the BIRADS lexicon. To the extent of our knowledge our study is among the earliest studies that used Kaiser Score to sort breast cancers according to their molecular subtypes.

Limitations

First, the number of hormonal negative lesions was limited among our lesions. Second, further studies are needed to assess the feasibility of the Kaiser Score descriptors solely or in association with the well-known BIRADS classification for breast cancer histological and immunological subtyping.

Conclusions

MRI BIRADS Lexicon descriptors are useful for molecular differentiation of breast cancer. Luminal A cancers frequently appear as mass lesions with irregular shape and border with rim enhancement while Luminal B cancers appear frequently show spiculated margin with irregular shape and dark internal septations. TN mass showed round shape, smooth border, and rim enhancement. As for Her2neu lesions non mass enhancement was more dominant.

Kaiser score improved categorization of certain subtypes as TN lesions which were upgraded into BIRADS 5, it also showed moderate interobserver agreement with BIRADS lexicon when used for retrospective assessment of breast cancer molecular subtyping.

Abbreviations

MRI	Magnetic resonance imaging
BIRADS	Breast imaging reporting and data system
ACR	American College of Radiology
FOV	Field of view
SPAIR	Spectral attenuated inversion recovery
TN	Triple negative
ER	Estrogen receptor
PR	Progesterone receptor
Her2neu	Human epidermal growth factor receptor 2
TIC	Time intensity curve

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Author contributions

FAS performed the methodology design, validation and statistical data analysis; NS and AK performed reviewing; DB performed writing and editing. All authors read and approved the final manuscript.

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Availability of data and materials

The data used in this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Written informed consent was waived from our institutional review board (IRB). IRB approval no: MD.18.04.36.

Consent for publication

The work described has not been published before.

Competing interests

The authors have no relevant conflicts of interest to disclose.

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