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Can the abbreviated MRI protocol replace the standard full protocol in the detection and characterization of breast non-mass enhancement?

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Abstract

Background Breast MRI full diagnostic protocol (FDP) showed great value in detecting and characterizing non-mass enhancement (NME); however, it is costly and time-consuming. MRI abbreviated protocol (AP) showed comparable accuracy to FDP in various indications but has not been specifically tested in NME. Our study purpose is to assess the accuracy of the AP in the detection and characterization of breast NME in comparison with the FDP and to perform time analysis of the AP.

Methods Patients who demonstrated NME in dynamic contrast-enhanced MRI were included to be assessed using AP and FDP. Image analysis was performed blindly and independently. Firstly, reconstructed images from the pre- and first post-contrast T1WI (first maximum intensity projection and subtraction) were made available as AP. Later, the time/signal intensity curve and remaining images of the FDP were added to the assessment. Both protocols were compared regarding acquisition time, interpretation time, BI-RADS scores and accuracy in the detection and characterization of NME in correlation to histopathology and/or follow-up. Validity statistics, Cohen-Kappa and ROC curve were used.

Results Fifty-nine NME lesions were identified. AP acquisition and interpretation times were significantly shorter than those of the FDP (3.3 vs. 35 min) and (45 "25–75 s" vs. 108 "80–150 s") ($P < 0.001$), respectively. There was almost perfect agreement between the two protocols in the BIRADS grading of NME ($k = 0.950$, $P < 0.001$). In ROC curve analysis, the FDP was insignificantly more accurate than the AP (84.8% vs. 81.4%, $P = 0.144$).

Conclusions Breast MRI-AP is comparable to the FDP in the detection and characterization of breast NME with advantageous time saving.

Keywords Breast, MRI, Abbreviated protocol, Non-mass enhancement

Background

With the development of the Breast Imaging Reporting and Data System (BI-RADS) lexicon for MRI, in addition to the mass and focus, a new term was introduced for the description of breast lesions, called non-mass enhancement, which stands for enhancement of an area that is neither a mass nor a blood vessel and having no space-occupying effect [1].

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In the general population, the prevalence of non-mass-breast enhancement is much lower than mass enhancement (13% vs. 76%). However, 57% of the non-palpable invasive breast cancers were presented with non-mass enhancement in MRI ensuring the effective use of breast MRI in breast cancer detection. Unfortunately, the limited availability of MRI limits its use as the second-line imaging method to solve the diagnostic problem in case of equivocal findings in mammography and/or ultrasound [1, 2].

The abbreviated breast MRI is an emerging technique in clinical practice, especially for screening purposes. The use of AP in the detection of breast cancer has gained increasing attention to save cost and time with substantially preserved accuracy [3]. Previous studies that advocated the use of the AP were based on the fact that invasive breast cancers and high-grade DCIS tend to enhance early due to the associated increase of angiogenesis and vessel permeability, while benign lesions frequently enhance later with gradually increased background parenchymal enhancement [4–6].

The feasibility of the AP in breast cancer detection was reported by Moschetta et al. [7] study, which concluded that the image acquisition and interpretation time could be significantly reduced without a negative impact on the diagnostic accuracy with brief emphasis on the NME. However, other studies proposed that the areas of NME have normal breast parenchyma from which the tumor can easily derive nutrition with less tumor neovascularization. Therefore, cancers presenting as NME may be more difficult to identify by the AP than cancers presenting as masses [6].

To our knowledge, the accuracy of the MRI-AP in the assessment of breast NME has not been sufficiently studied. The current study aimed primarily to assess the accuracy of the MRI AP in the detection and characterization of breast NME in comparison with the FDP, secondarily to perform time analysis of the AP.

Methods

Study population

This cross-sectional prospective study has been performed between April 2019 and January 2023 on female patients referred to the diagnostic radiology department of university hospital for DCE breast MRI with different indications (screening, problem solving and preoperative assessment). Patients who demonstrated NME were included to be assessed using AP and FDP. Both protocols were compared in correlation to histopathology and/

or follow-up. Patients with no detectable NME, missed during follow-up and those with incomplete MRI protocol or bad-quality MRI images were excluded from the study.

MRI protocol

All MRI examinations were performed using 1.5 Tesla systems (Siemens Magnetom Semptra, Siemens Healthineers, Germany), and the four-channel phased array breast coil was used. Patients were examined in prone position, with arms by the sides of the body, and both breasts were well placed and fitted into the coil to avoid distortion of its contour. The MRI protocol included localizer axial fast spoiled gradient echo, axial T₁WI (repetition time/echo time “TR/TE” = 540/10 ms, field of view “FOV” = 400 mm, slice thickness “ST” = 3 mm, matrix = 340 × 512), axial T₂WI (TR/TE = 4500/120 ms, FOV = 380 mm, ST = 3 mm, matrix = 340 × 512). Axial T₂ with fat suppression (TR/TE = 3600/80 ms, FOV = 380 mm, ST = 3 mm, matrix = 340 × 512) and axial diffusion weighted imaging (DWI) (TR/TE = 1500/80 ms, FOV = 460 mm, ST = 4.5 mm and matrix = 340 × 512) were also acquired before dynamic sequences with a spin EPI (echo-planner imaging) in the axial plane, and sensitizing diffusion gradients were applied along the *x*, *y* and *z* directions with *b* values of 50, 400 and 800 s/mm². Finally, the intravenous contrast agent (Gadolinium-dimeglumine) (Gd-DTPA) (Magnevist, Schering AG Berlin, Germany) was injected using an automatic power injector at a dose of (0.1 mmol/kg) and a rate of 2 ml/s, followed by a 20-ml saline flush administered. Multiphasic (5 phases) dynamic post-contrast sequences were done, first phase was done after 60 s, each phase lasts for about 1 min with 18-s lag time between phases.

Data processing

Image post-processing techniques were applied for all MRI examinations. Subtraction images were obtained by subtraction of the non-enhanced T1 WI images from the contrast-enhanced images. MIP images were also obtained from the contrast-enhanced images.

Image analysis

In two separate sessions, image analysis was performed blindly and independently. In the first session, the reconstructed images from the pre- and first post-contrast T1WI (first MIP and subtraction) were assessed as an

AP. In the subsequent session, time/signal intensity curves were obtained and then all images of the FDP were made available to the assessment. BIRADS category was assigned for each lesion in AP and FDP separately. Both AP and FDP protocols were compared regarding the acquisition time, interpretation time and cancer yield, accuracy in staging in correlation to the histopathological and operative findings.

Histopathological examination and follow-up

All included cases underwent histopathological examination and/or follow-up according to their BIRADS. BIRADS 2 and 3 lesions were subjected to two annual MRI follow-up.

Statistical analysis

Data were collected and analyzed using the statistical package for social sciences, version 20 (IBM Corp., Armonk, New York, USA). Continuous data were expressed in the form of mean, SD, or median (range), frequency (percentage), FP: false positive; and FN: false negative. The acquisition time, interpretation time and diagnostic accuracy of the AP were investigated and compared to those of the FDP using the ROC curve and the area under the curve (AUC, 95% CI) analysis.

Results

Fifty-nine NME lesions were detected in 56 patients (3 of them were presented with bilateral NME lesions) with mean age 38.59 ± 11.07 (range 27–69) years. Twenty-four patients were referred for screening, 27 for problem solving and 5 for preoperative assessment. Histo-pathological examination was done for 27 lesions, while 32 lesions were subjected to follow-up. Based on histopathological results, 17 lesions were malignant (9 of them were invasive carcinoma) (Fig. 1), whereas the remaining 10 lesions were benign. While those subjected to follow-up 12 of them showed complete resolution and the remaining had no significant changes (Table 1) (Fig. 2).

MRI findings of NME lesions (Table 2)

Distribution

Seventy percent of the histopathologically proven malignant NME had diffuse (Fig. 1) or segmental distribution (Fig. 3) in MRI with equal percentages (35.3% each), while 43% of the detected benign NME showed regional distribution, with a statistically significant difference between the MRI distribution of the benign and malignant lesions (P value = 0.001) (Table 2).

Enhancement pattern

The majority (70.6%) of the MRI detected malignant NME were heterogeneous, while 50% of the benign lesions showed homogenous pattern of enhancement (P value = 0.006) (Table 2).

Time-intensity curve

There was a high statistically significant difference between the type of time-intensity curve in the MRI-detected benign and malignant NME where the majority of the benign NME lesions exhibited type I curve (Fig. 1), while most of malignant NME were presented as type II curve (Table 2).

DWI and apparent diffusion coefficient value (ADC)

Restriction, at b -value 1000 s/mm^2 , was observed in 27 lesions; among malignant lesions 15 (88.2%) had diffusion restriction (P value < 0.001).

With the best cutoff value $1.2 \times 10^{-3} \text{ mm}^2/\text{s}$ has a sensitivity of 76.5% a specificity of 64.3% (P value = 0.005) (Table 2).

BI-RADS grading of the MRI detected NME by the FDP and AP

There was perfect agreement between FDP and AP in the distribution of BI-RADS 2 and BI-RADS 5 NME lesions. However, there was insignificant difference in the distribution of BI-RADS 3 and BI-RADS 4 (as two lesions were graded as BI-RADS 3 in the AP but upgraded to BI-RADS 4 during the assessment of the FDP) with almost perfect total agreement between the two protocols in the BIRADS grading of the included NME lesions ($k = 0.950$, $P < 0.001$) (Table 3).

The acquisition and interpretation times of the AP were significantly shorter than those of the FDP (3.3 vs. 35 min) and (45 ± 10.29 "range: 25–75 s" vs. 108 ± 16.41 "range: 80–150 s"), respectively, with a statistically significant difference between both protocols (P value < 0.001) (Table 4); also all statistical parameters of the FDP were higher than those of the AP yet with no statistically significant difference between the two MR protocols in the AUCs where the accuracy of the full protocol was only a little bit higher than that of AP (84.8% vs. 81.4%, respectively, $P = 0.144$) (Table 5).

Discussion

NME is enhancement of an area that is neither a mass nor a blood vessel, does not have space-occupying effect, and can be distinguished from the enhanced surrounding

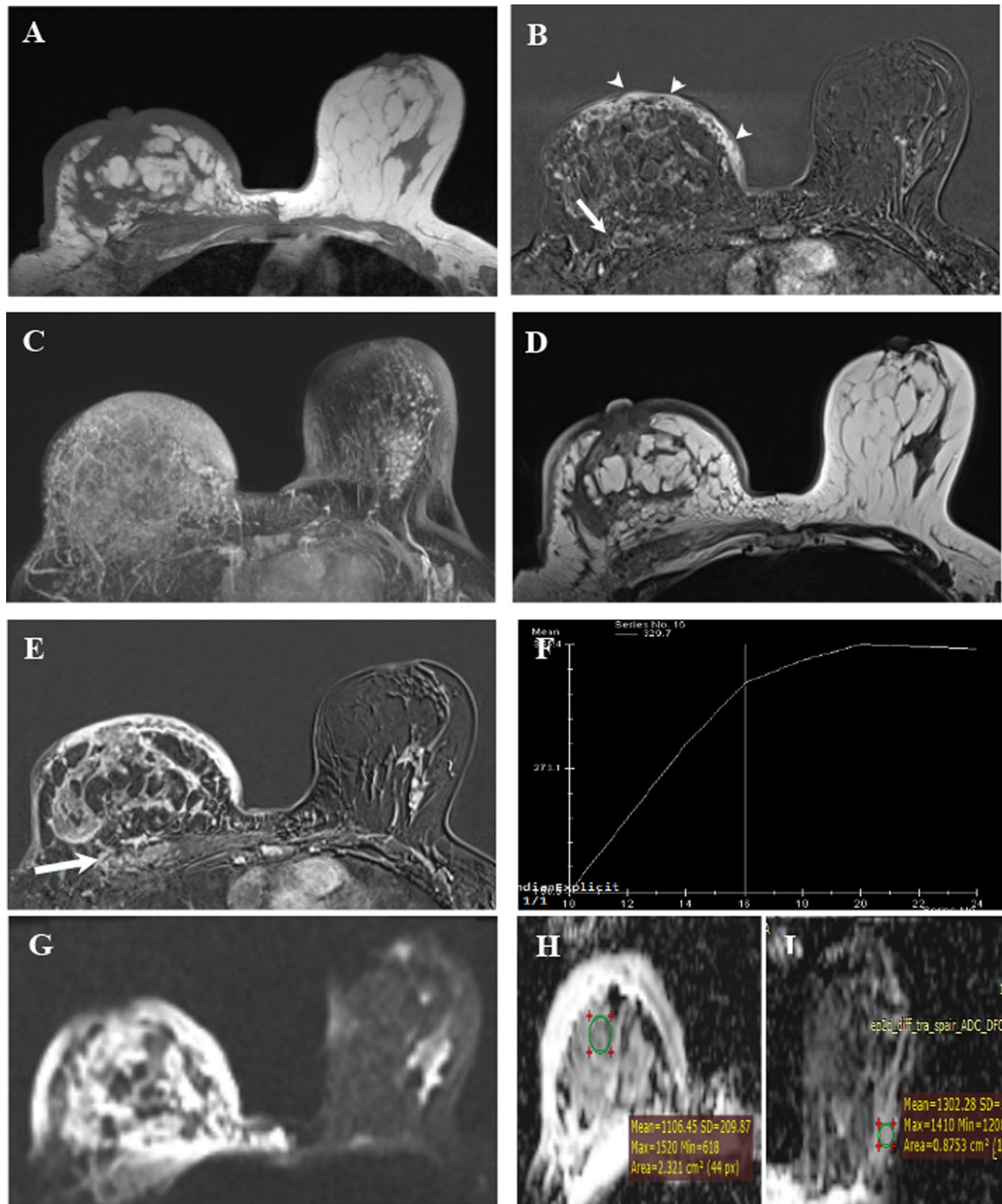


Fig. 1 Thirty-year-old woman referred with right unresolved mastitis (problem-solving indication). **a** Precontrast T1WI showed diffuse skin thickening and edema, no masses. **b** First post-contrast subtraction showed diffuse heterogeneous non-mass enhancement with enhancement of the skin (arrow heads) and retromammary muscle (arrow). Contralateral breast showed segmental heterogeneous non-mass enhancement; these findings could be seen in 1st MIP **(c)**. **d** T2WI showed no masses. **e** Late post-contrast subtraction confirmed pectoralis muscle invasion (arrow); contralateral non-mass enhancement showed type II kinetic curve. **(f)** The two lesions showed restricted signal in DWI (b -value 800 s/mm²) **(g)** with ADC values = 1.1×10^{-3} mm²/s for the right breast lesion **(h)** and 1.3×10^{-3} mm²/s for the left one **(i)**. The right breast lesion interpreted as BIRADS V, while the left lesion interpreted as BIRADS IV in both protocols. True cut needle biopsy of right breast revealed invasive carcinoma, while left breast lesion revealed DCIS

Table 1 Demographic data, pathological findings and follow-up

Parameter	N= 56 patients (59 lesions)
<i>Age (years)</i>	
Mean (range)	38.59 + 11.07 (27–69)
<i>Indications</i>	
Screening	24
Problem solving	27
Preoperative	5
<i>Pathological findings</i>	
Malignant lesions	27/59
Invasive carcinoma	17/27
IDC	9
Non-specified	4
DCIS	5
Inflammatory carcinoma	3
<i>Benign lesions</i>	
Focal adenosis	10/27
Periductal mastitis	3
Mixed inflammatory infiltrates	2
Hyperplasia	3
Two annuals follow-up of 32 non-mass lesions. Confirms benign nature by	2
Stationary coarse	32/59
Complete resolution	20
	12

normal breast parenchyma [1, 8]. Hence, NME represents a critical challenge in the interpretation of breast MRI because there is normal breast parenchyma in the NME lesion, from which the tumor cells can easily derive their nutrition with less tumor neovascularization. Consequently, dynamic enhancement parameters had limited value [1, 9, 10].

Therefore, we paid NME a special concern and specified statistical analysis and the aim of the current study was to assess the accuracy of the MRI AP in the detection and characterization of breast NME in comparison with the FDP and to perform time analysis of the AP.

When comparing the AP to the FDP of MRI breast we found that the acquisition time of the AP; consisting of unenhanced T1W sequence, one post-contrast T1W sequence (60 s after contrast injection), a single subtraction and MIP images, is significantly shorter “by about 31.7 min” than that of the FDP. By using the same AP employed in the current study, Kuhl et al. [2] and Oldrini et al. [3] observed nearly equivalent acquisition time (3 min). Differently, Mango et al. [10]

used the abbreviated MR protocol proposed by Kuhl et al., and they observed that the acquisition time was 10–15 min. The shorter acquisition times of the previous and current APs will encourage the widespread use of breast MRI by reducing patient discomfort, thus enabling the performance of a higher number of MRI examinations.

The post-processing and interpretation time of our AP ranged from 25 to 75 s with an average of 45 s, which is significantly longer than that of the FDP. This is close enough to the result of Mango et al. [10] (44 s), but much longer than that of Moschetta et al. [11] (30 s) who used a different AP, including the pre-contrast (T2-weighted TSE, STIR, pre-contrast THRIVE) and the third post-contrast THRIVE sequences, and the corresponding subtracted and MIP images. On the other hand, Oldrini et al., who utilized the same AP of the current study, have found that the mean interpretation time for the senior physician was about 60 s [3].

In agreement with Aydin [12], the majority of the histopathologically proven malignant NME lesions in the current work exhibited segmental or diffuse distribution. Furthermore, in consistence with the present data, yang et al. [1], Wilhelm et al. [13] and Liu et al. [8] stated that segmental distribution was the commonest among malignant lesions, while the most frequent pattern of enhancement among malignant lesions was heterogeneous pattern. In contrast, the clustered ring pattern was significantly higher in the malignant NME compared to the benign lesions in previous studies [1, 12].

In the present study, the most frequent dynamic curve among malignant lesions was the type II curve which is equivalent to Yang et al. [1] and Aydin [12] studies, but in contrast to Liu et al. [8] study which concluded that the wash-out dynamic curve is the uppermost indicator for malignancy. In addition, Choudhery et al. [9] concluded that kinetic enhancement curves did not demonstrate a statistically significant relationship with the lesion’s pathologic features.

DWI parameters play an important role in differentiating malignant breast lesions; however, its role in NME was variable in different previous studies. In the current study, diffusion restriction was significantly higher in malignant lesions which goes in agreement with [12] but in contrast to Liu et al. [8] who found a statistically non-significant difference in diffusion restriction, while regarding ADC cutoff value, in the current study

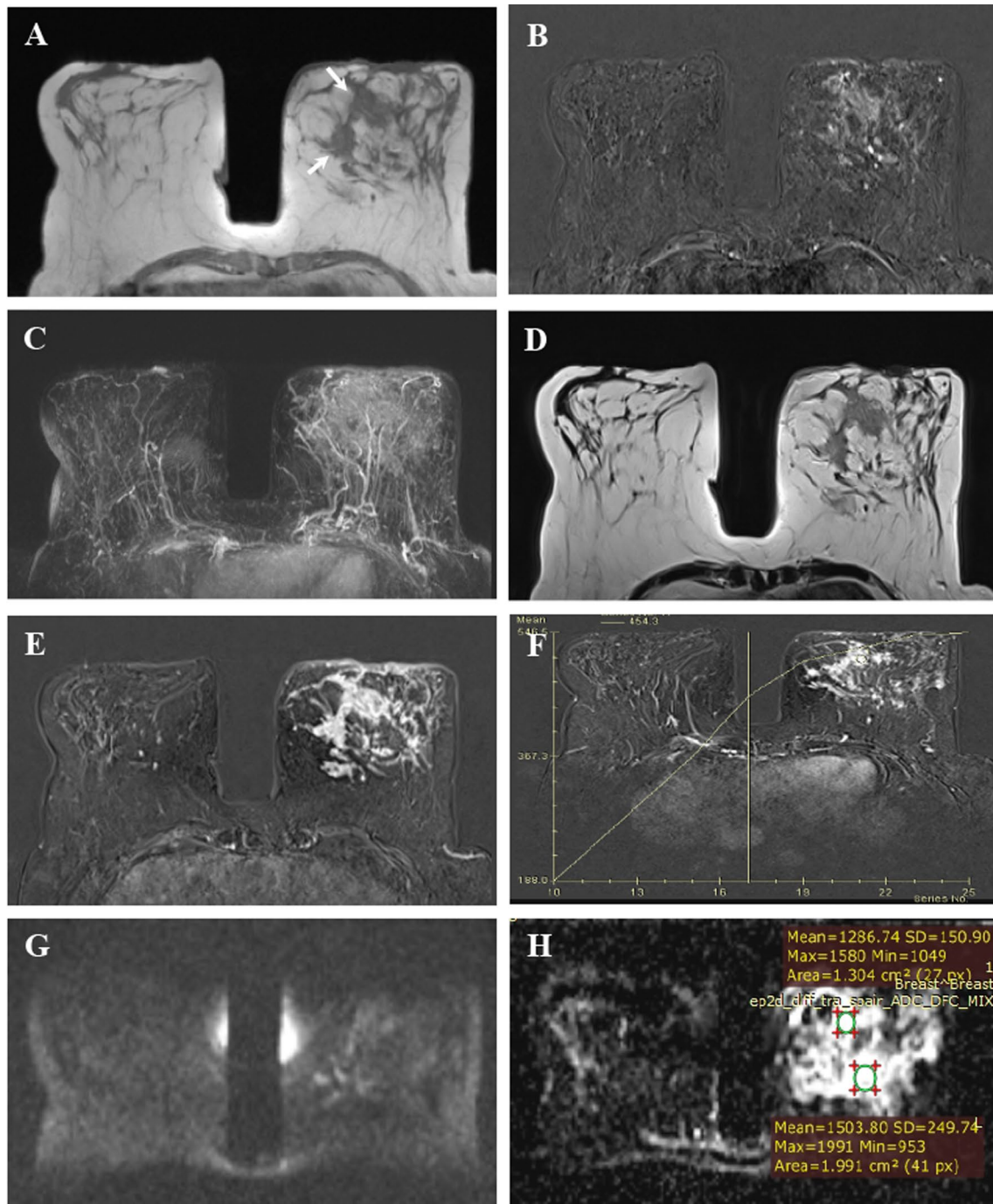


Fig. 2 Forty-four-years-old woman presented with left breast pain and tenderness (problem-solving indication). Pre-contrast T1WI (a) demonstrating multiple non-circumscribed areas of abnormal hypointense signals occupying the lower quadrants of the left breast (arrows) associated with minimal skin thickening. Faintly detected on 1st MIP (b). c First post-contrast subtraction showing faint non-mass enhancement with multiple regions distribution and homogenous pattern. (d) T2WI revealed intermediate signal. e Increased intensity of non-mass enhancement in late post-contrast subtraction, making type I kinetic curve. Facilitated signal in DWI at b value 800 s/mm² (g), with high ADC values at two different parts. 1.29 and 1.50×10^{-3} mm²/s (h). Interpreted as benign inflammatory condition BIRADS III by both protocols. Medical treatment and two annual follow-up MRI confirm benign nature

Table 2 MRI findings of NME in correlation to histopathology

Distribution	Malignant (n = 17)	Benign (n = 42)	P value*
Diffuse	6 (35.3%)	0 (0.0%)	0.001
Focal	0 (0.0%)	9 (21.4%)	
Linear	2 (11.8%)	3 (7.1%)	
Regional	0 (0.0%)	18 (43%)	
Multiple regions	3 (17.6%)	9 (21.4%)	
Segmental	6 (35.3%)	3 (7.1%)	
<i>Pattern</i>			
Homogenous	5 (29.4%)	21 (50.0%)	0.006
Heterogeneous	12 (70.6%)	12 (28.6%)	
Clumped	0 (0.0%)	9 (21.4%)	
<i>Kinetic curve</i>			
Type I	0 (0.0%)	36 (85.8%)	< 0.001
Type II	10 (58.8%)	3 (7.1%)	
Type III	7 (41.2%)	3 (7.1%)	
<i>Diffusion restriction</i>			
Present	15 (88.2%)	12 (28.6%)	< 0.001
Absent	2 (1.8%)	30 (71.4%)	
<i>ADC value $\times 10^{-3}$ mm²/s cutoff point</i>			
≤ 1.21	13 (76.5%)	15 (35.7%)	0.005
> 1.21	4 (23.5%)	27 (64.3%)	

*Chi-square test was used to compare the proportion difference between group

*Significant test results were considered when P value was < 0.05, P value < 0.001 indicating high significance

a value of $\leq 1.2 \times 10^{-3}$ mm²/s was the best for detection of malignant lesions with sensitivity and specificity of 76.5% and 64.3%, respectively; this was near equivalent to that concluded by Liu et al. who found an ADC value of $\leq 1.3 \times 10^{-3}$ mm²/s is the best for predicting malignant NME lesions with sensitivity and specificity of 83.9% and 45.2%.

The current results state almost perfect agreement between the AP and FDP in the BIRADS grading of the included NME lesions, to our knowledge no previous studies compared BIRADS grading of NME between the two protocols.

Heacock et al. [14] study was the only one that reported concisely the accuracy of the MRI-AP in the interpretation of breast NME when they analyzed 107 women who had uni-focal breast cancer and showed that breast cancers presenting as NME may be more difficult to identify on the MRI-AP than cancers presenting as masses. In the current study, we detected a larger number of NME than those discovered in the study population of Heacock et al. (59 vs. 5 NME

lesions, respectively). Nine of the currently detected NME were overlooked as malignant in both AP and FDP; three were regional homogenous reaching the nipple and pathologically proved to be periductal mastitis, while the remaining 6 lesions were pathologically proved to be adenosis where 4 of them were segmental heterogeneous and two were linear clumped. Moreover, the AP missed two linear homogenous NME lesions (pathologically proved DCIS) that were picked up by FDP where lesions became more obvious in late phases.

Hence, the statistical indices of the FDP were slightly higher than those of the AP but with no statistically significant difference between the diagnostic efficacy of the two MR protocols. Yang et al. who conducted their study to explore and evaluate the new malignant predictors of breast NME by analyzing 84 NME lesions detected in 422 consecutive women underwent the standard breast 3.0 T MRI, concluded that the initial signal enhancement ratio and the peak enhancement were not significantly different in discriminating benign and malignant NME of the breast [1]. This means that there is no significant difference between the diagnostic accuracy of the AP and FDP, which is in concordance with the current study results.

Limitations

The current study has two limitations. First, the small sample size might be explained by the lower prevalence of non-mass breast enhancement in the general population compared to mass enhancement. Second, only the first post-contrast phase was included in the current AP; hence, the dynamic enhancement curve could not be obtained, which might reduce the ability of the AP in discriminating some of the malignant NME lesions. Therefore, we recommend the inclusion of the three contrast-enhanced phases in the AP to study the kinetic enhancement of the lesions.

Conclusions

The AP of breast MR can be used as a time and cost-saving alternative with comparable sensitivity to that of the FDP in the characterization of breast NME lesions in patients undergoing MRI for purposes of screening, problem solving or preoperative assessment because the categorization of breast NME lesions depends largely on their morphological criteria rather than their enhancement kinetics.

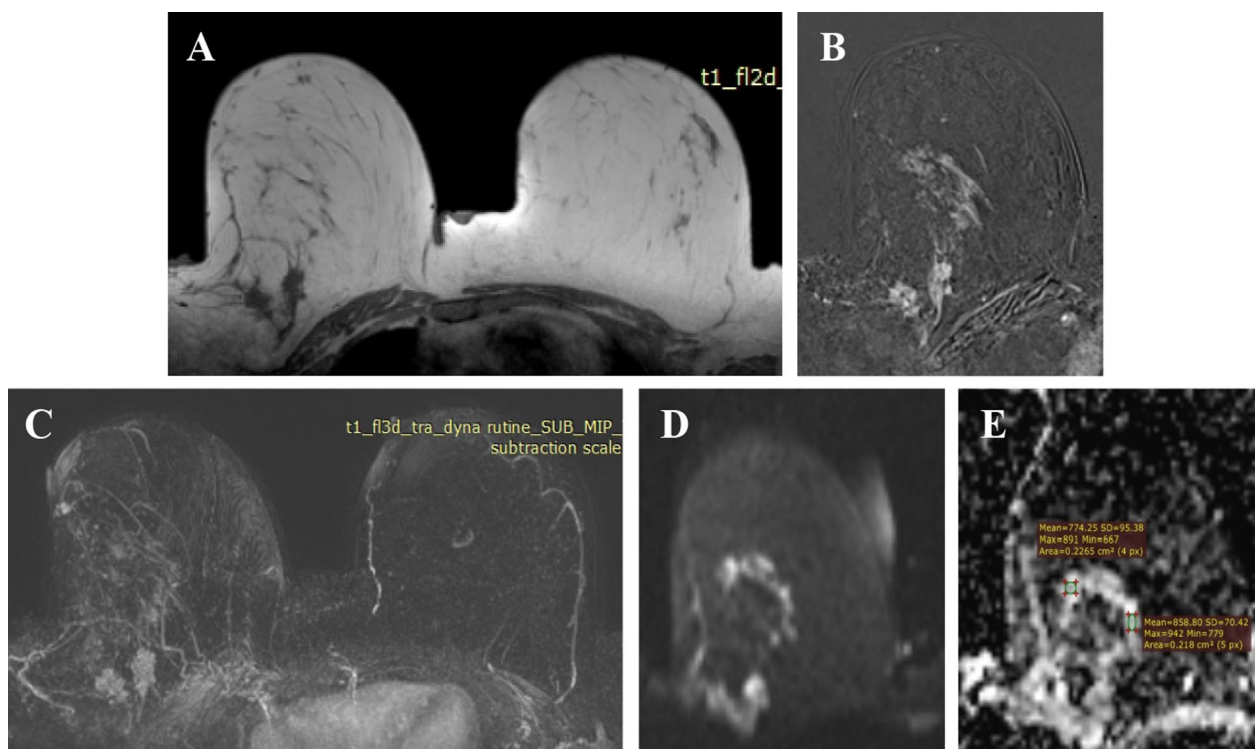


Fig. 3 Thirty-four-years-old woman referred with pathologically proved right breast multifocal IDC (preoperative assessment indication). Precontrast T1WI (a) showed two hypointense spiculated mass lesions at the UOQ. b First post-contrast subtraction showed rapid intense enhancement of the previously described mass lesions with adjacent heterogeneous segmental non-mass enhancement; all these findings are detected in 1st MIP. Adjacent non-mass enhancement showed restricted signal in DWI (b-value 800 s/mm²), (d) with ADC values=0.77 and 0.86 × 10⁻³ mm²/s, (e) left intramammary L.N is noted. Multicentricity was interpreted. After these concluded findings the surgical plan was modified from right conservative breast surgery (CBS) to modified radical mastectomy (MRM)

Table 3 BI-RADS grading of the MRI detected NME by the FDP and AP

	FDP BI-RADS				Total	
	BI-RADS 2	BI-RADS 3	BI-RADS 4	BI-RADS 5		
AP BI-RADS	BI-RADS 2	23	0	0	0	23
	BI-RADS 3	0	10	2	0	12
	BI-RADS 4	0	0	21	0	21
	BI-RADS 5	0	0	0	3	3
Total	23	10	23	3	59	
Kappa agreement	0.950*					
P value	<0.001					

*Degree of agreement calculated by Fleiss' kappa (k): 0.81–1.0 almost perfect agreement

Table 4 Acquisition and interpretation times of the abbreviated and full diagnostic MRI protocols

	Full protocol	Abbreviated protocol
Acquisition time	35 min	3.3 min
Interpretation time	108 s ± 16.41 (80–150)	45 s ± 10.29 (25–75)
P value	<0.001	

Table 5 Validity measures of the abbreviated and full diagnostic MRI protocols in the detection and characterization of non-mass enhancement

	Full protocol	Abbreviated protocol
Kappa agreement	0.679	0.601
Validity measures	Value	Value
Sensitivity, %	(17/17)100.0%	(15/17)88.3%
Specificity, %	(33/42)78.6%	(33/42)78.6%
PPV, %	(17/26)65.4%	(15/24)62.5%
NPV, %	(33/33)100.0%	(33/35)94.3%
Accuracy, %	84.8%	81.4%
AUC	0.893 (0.812–0.974)	0.834 (0.718–0.950)
P value	=0.144	

Abbreviations

- MRI Magnetic resonance imaging
- FDP Full diagnostic protocol
- NME Non-mass enhancement
- AP Abbreviated protocol
- DCE Dynamic contrast enhanced
- MIP Maximum intensity projection
- BI-RADS Breast Imaging-Reporting and Data System
- ROC curve Receiver operating characteristic curve

TR/TE	Repetition time/time to echo
FOV	Field of view
ST	Slice thickness
DWI	Diffusion weighted imaging
EPI	Echo-planer imaging
SD	Standard deviation
AUC	Area under the curve
CI	Confidence interval
CBS	Conservative breast surgery
MRM	Modified radical mastectomy

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Author contributions

A.S.H, A.H.A, H.A.Y and E.A suggested the idea and contributed to the design and construction of the main outlines of the study methodology to reach a conclusion. A.S.H, A.H.A, S.H and M.M performed the technical parts of the study and contributed to the interpretation of the results. A.S.H, H.A.Y and A.H.A. performed the numerical calculations and statistical analysis of data. A.S.H, A.H.A, H.A.Y and E.A contributed discussion of the results and provided a draft. A.S.H and A.H.A wrote the manuscript with input from all authors. A.H.A, S.H and M.M contributed revision of spelling, grammar and intellectual contents of the manuscript. E.A and H.A.Y took the responsibility of organizing and supervising the course of the work. All authors agreed to the final version of the manuscript and provided final approval to submission.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All patients participated in this study signed an informed written consent for participation in this research. Ethical considerations: Risk Benefit assessment for all patients was indicated for the examination during this study. Confidentiality: All patients' data were confidentially kept. The research was done by scientifically qualified and trained personnel. The procedures included in this study had been already used in hospitals and centers in and outside Egypt. This study had approval from Assiut University, Egypt, Faculty of Medicine Research Ethics Committee, reference number (IRB: 17200312).

Consent for publication

All patients participated in this study signed an informed written consent for publication of their data in this research.

Competing interests

Authors declare that they have no competing interests.

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