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Original article

Abbreviated breast MRI for evaluating breast cancer before initiation of neoadjuvant chemotherapy: A cross-sectional study

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ABSTRACT

Background: Although, there are accumulating evidence about diagnostic role of abbreviated breast magnetic resonance imaging (MRI) in screening setting, the implementation of abbreviated MRI in staging of breast cancer has been poorly elucidated.
Objective: To evaluate the diagnostic performance of abbreviated breast MRI in estimating extent of disease before initiation of neoadjuvant chemotherapy.
Methods: A total of 54 patients with biopsy-proven main lesion referred to evaluate by standard protocol breast MRI before initiation of neoadjuvant chemotherapy were retrospectively enrolled. From a standard protocol, a data set of abbreviated protocol consisting fat-saturated T1-weighted (T1W) pre-contrast and first two fat-saturated T1W post-contrast series with reconstruction of their subtraction including maximum intensity projection (MIP) were obtained and interpreted. The concordance rate of abbreviated with standard protocol (as a reference standard) were compared. Diagnostic accuracy, sensitivity, specificity, and positive and negative predictive value were calculated, as well.
Results: The maximum size of the main mass was 38.6 ± 17.3 and 40.7 ± 17.9 for abbreviated and standard protocol, respectively. All of the main mass was detected by abbreviated protocol with 100% concordance. Concordance was 98.1% and 94.4% in terms of multifocal/multicentric status and for estimating of NME, respectively. The abbreviated protocol has high sensitivity and specificity with more than 90% value regarding main mass detection, measurement of the maximum size of the main mass, determination of multifocal/multicenter status and NAC involvement.
Conclusion: Abbreviated protocol may be a reliable surrogate for standard protocol breast MRI in evaluating extent of breast cancer.

1. Introduction

Breast cancer is the most common cause of malignancy in women worldwide and is regarded as one of the leading causes of cancer related mortality and morbidity [1]. The prognosis of breast cancer has been improved owing to rapid advancement in imaging modalities for screening and detection of cancer, as well as great progression in pharmacological and surgical treatments [2].

Historically, neoadjuvant chemotherapy is one the mainstay of breast cancer treatment. Neoadjuvant chemotherapy, has not only been used for managing locally advanced breast cancer [3], but also has been recently applied for treating early breast cancer in the era of trend for breast conservative surgery [4]. More importantly, recent evidence showed that neoadjuvant chemotherapy could be employed to monitor response and tailor treatment especially in TNBC and HER-2 positive breast cancer [5,6]. Given widespread administration of neoadjuvant chemotherapy, breast imaging including mammography, ultrasound and MRI is mandatory to evaluate the disease extent before the initiation of neoadjuvant chemotherapy [7]. Hence, precise response monitoring of this regimen is principally dependent on the baseline imaging

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characteristics of breast cancer to compare tumor changes, radiologically, during and after the completion of neoadjuvant chemotherapy [8].

MRI is highly sensitive and accurate in assessing the size of breast cancer and in identifying multifocal and multicentric tumors [9,10]. Standard protocol MRI is the favored imaging modality for evaluating extent of disease and leveraging treatment strategy. However, some concerns have been remained regarding the widely-used standard protocol MRI due to inappropriate time-consuming process of imaging acquisition and subsequently longer interpretation time [11].

Abbreviated MRI has been introduced in the screening and diagnostic setting in order to reduce the acquisition time, interpretation length and in turn, optimizes cost-effectiveness and consequently outspreads the accessibility of this approach with comparable sensitivity and specificity to standard protocol MRI [12,13]. To the best of our knowledge, there are few reports about abbreviated MRI in evaluating breast cancer before initiation of neoadjuvant chemotherapy particularly to determine whether this protocol has acceptable accuracy for assessing the extent of disease as a surrogate to standard protocol [14]. Verification of this assumption could be influential in real-world clinical practice, since abbreviated breast MRI might be potentially implemented as a single reliable modality for both detection of cancer and evaluation of the disease extent.

Accordingly, the goal of the current investigation was to elucidate the accuracy of abbreviated MRI in evaluating extent of breast cancer in subjects who are candidates for neoadjuvant chemotherapy.

2. Materials and methods

2.1. Study population

This retrospective study was reviewed and approved by institutional board and written informed consent was waived due to the retrospective nature of the investigation. The current study was performed in Imam Khomeini Hospital (a tertiary referral center), Tehran, Iran. The breast imaging center database of our institution was searched from January 2018 to May 2021 for consecutive cases with biopsy proven breast cancer who underwent standard protocol breast MRI before initiation of neoadjuvant chemotherapy. Out of 66 subjects, those with marked artifact (due to motion or clips) on their images (n = 7), and those showed considerable post-biopsy changes (such as hemorrhage) perturbing quality of MRI images (n = 5), were excluded. Finally, a total number of 54 subjects recruited for the analysis.

2.2. MRI protocol and image analysis

All MRI examinations were performed using a GE Discovery MR750 3 T MRI scanner (GE Healthcare, Waukesha, WI, USA) with dedicated multichannel 16-row breast coil. We used the sequences of both abbreviated and standard protocols the same as our previous study [15].

The standard protocol MRI consisted of axial fat-suppressed T2-weighted image (T2W), axial T1-wieghted image (T1W), four post-contrast dynamic phases and diffusion weighted imaging (DWI) with apparent diffusion coefficient (ADC) maps. Also, subtraction and maximum intensity projection (MIP) images were generated automatically on picture archiving and communication system (PACS). From the standard protocol, some sequences were selected for interpretation as the abbreviated MRI. This data set comprised pre-contrast T1W image, first and second post-contrast phases and MIP. Both of the standard and abbreviated protocols were anonymized to interpreting radiologists.

Two expert fellowship-trained radiologists (15 and 10 years of experience) independently evaluated the standard and abbreviated protocols. Both interpreting radiologists were only aware that the participants harbor biopsy proven breast cancer. At first, radiologists evaluated the abbreviated protocol and to minimize potential recall bias, evaluation of the standard protocol was preformed 6 weeks later.

The following imaging features were documented for extent of disease: detection of the main mass, measurement of the maximum size of the main mass, identification of the suspected multifocal or multicenter status, determination of the presence/absence of non-mass enhancement (NME) included focal, clumped, clustered ring, linear, or segmental enhancement pattern, evaluation of the nipple-areolar complex (NAC) invasion in a dual form as normal or suspected/positive according to the distance of tumor extension in 10 mm or less relative to NAC and interrogation of the axillary lymph node involvement in a binary fashion as normal or suspected/positive based on the detection of at least one of the abnormal morphology criteria consisting cortical thickening, abnormal (round) shape, and/or hilar replacement.

3. Theory/calculation

Descriptive analysis was performed for the subjects' characteristics and denoted as mean ± standard deviation for continuous variables and number (percentage) for categorical variables. The Cohen's kappa (κ) coefficient was employed to determine the inter-rater agreement (IRA) between two radiologists. Kappa < 0 indicates no agreement, 0–0.20 as poor, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1 as excellent agreement. During the designing of the study, we postulated priori if there was excellent agreement between two raters, the results of more experienced radiologist were applied for the final analysis. The standard MRI protocol was deemed as the reference standard for assessing the imaging features regarding extent of malignancy. The data of abbreviated protocol are compared with the standard counterpart; Concordance was deemed if both protocols indicated the same results about the various imaging characteristics of the tumor extent. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated. All statistical analyses were performed using SPSS (IBM Corp., Armonk, NY, USA) version 26.

4. Results

4.1. General Features

Out of 54 patients (mean age 46.02 ± 8.89) with biopsy proven breast cancer, forty patients (74%) diagnosed as invasive ductal carcinoma (IDC) followed by DCIS in 7 (13%) cases and IDC/DCIS in 7 (13%) cases. The detailed characteristics of all participants are presented in

Table 1
Characteristics of the study subjects.

Variables	Values
Age	46.02 ± 8.89
Fibroglandular tissue	
Almost entirely fatty	4 (7.4)
Scattered fibroglandular tissue	21 (38.9)
Heterogeneous fibroglandular tissue	22 (40.7)
Extreme fibroglandular tissue	7 (13.0)
Background parenchymal enhancement	
Minimal	26 (48.1)
Mild	19 (35.2)
Moderate	9 (16.7)
Marked	-
Associated findings	
None	26 (48.1)
Nipple retraction	1 (1.9)
Skin direct invasion	13 (24.1)
Skin thickening	8 (14.9)
Pectoralis muscle invasion	5 (9.3)
Architectural distortion	1 (1.9)
Main Mass Pathology	
IDC	40 (74.0)
DCIS	7 (13.0)
IDC+DCIS	7 (13.0)

Table 1. Excellent agreement (κ = 0.94–0.98, P < 0.001) was demonstrated between the two radiologists for all components of the disease extension. The mean total acquisition times for abbreviated and standard protocols were approximately 4 min and 30 min, respectively. Average interpretation times for abbreviated and standard MRI protocols were approximately 4 min, and 10 min, respectively.

4.2. Abbreviated MRI protocol and assessing extent of disease

Comparative results of all components of the disease extent are summarized in Table 2. The maximum size of main mass was 38.6 ± 17.3 and 40.7 ± 17.9 for abbreviated and standard protocol, respectively. Data regarding concordance and discordance between abbreviated and standard protocol was depicted in Table 3. The acceptable concordance was shown for measuring size of the main mass (90.7% concordance) when compared to standard protocol as the reference standard. All of the main mass was detected by abbreviated protocol with 100% concordance. Details of discrepant are following: Among patients, extent of disease was upgraded from unicentric in abbreviated protocol to multicentric in one subject when compared to standard protocol. Hence, concordance was 98.1% in terms of multifocal/multicentric status. In 5.5% of women, 3 undetected NME in abbreviated protocol was ranged in extent from 7 to 23 mm, accordingly concordance was 94.4%. The pattern of NME in these patients was linear (67%) and segmental (33%) in the reference standard. In terms of axillary adenopathy, two false positive (both of them were in range of 4–8 mm) and one undetected adenopathy was documented with size of 12 mm. Among 3 discordant cases regarding NAC invasion, two of which were false negative and one was overdiagnosed due to massive skin edema.

The diagnostic performance of abbreviated MRI protocol compared to the standard protocol is shown in Table 4 as regards all evaluated imaging characteristics for extent of disease. The abbreviated protocol has high sensitivity and specificity with more than 90% value regarding main mass detection, measurement of main mass size, determination of multifocal/multicenter status and NAC invasion.

5. Discussion

The aim of this retrospective observational study was to investigate the performance of the abbreviated protocol for evaluation of the extent of breast cancer compared to the standard protocol as the reference standard. The abbreviated MRI was able to detect all malignant main lesions and tended to show excellent sensitivity and specificity with highest levels of reliability for excluding/confirming the main tumor mass. Moreover, this protocol could be reliable with high value of specificity and sensitivity for evaluation of the disease extent especially about mean size of the main mass, additional multifocal and multicentric lesions, as well as NAC invasion.

After introducing of the abbreviated breast MRI by kuhl et al., several protocols were investigated to optimize this approach [16]. Our protocol consisted of T1 fat-saturated pre-contrast and first and second fat suppressed post-contrast series with their subtraction and MIP of the first two post-contrast sequences. Since some pervious reports indicated that using only the first post-contrast images could miss 15% of cancers, we used second post contrast images to minimize false negative results in low-grade breast cancers.

Although an accumulating body of evidence advocates the reliable diagnostic performance of the abbreviated breast MRI in a screening setting [17], limited data are available for the effectiveness of this modality in the evaluation of staging, disease extent and response to neoadjuvant chemotherapy. A previous study conducted by Mango et al. showed that abbreviated MRI is excellent in detecting breast cancer, consistent with our results [18]. Heacock et al. also found that the mean detection rate for all 3 different abbreviated protocols was more than 97% in 100 biopsy proven unicentric breast cancers which is comparable to the results of the current study [19]. All cancers were identified by at least one of three readers in the aforementioned report.

Identification of the additional multicentric and multifocal lesions are important for treatment planning [20]. Accordingly, it is invaluable to determine the diagnostic value of the abbreviated protocol in setting of multifocal/multicenter breast malignancies. In a study that investigated the abbreviated MRI in estimating extent of disease in 81 women with newly-diagnosed breast cancer, Le-felker et al. demonstrated that abbreviated MRI was able to detect all multifocal, multicentric diseases seen in 19% (15/81) of women to the same extent as the standard protocol [21]. The current study demonstrated that in 31 multifocal/multicentric disease, the abbreviated protocol only missed one case with 98% sensitivity. So, the abbreviated protocol could be reliably applied in identifying disease extension. Another study by Girometti et al., compared the abbreviated and the standard protocol for additional diseases during breast cancer staging in 87 patients with 89 biopsy-proven main lesions [22]. The authors showed that abbreviated MRI was comparable to standard MRI in staging additional breast cancers (multifocal, multicentric, and contralateral) which further indicates the imperative role of the shortened breast MRI protocol in the future clinical practice.

Our results showed the abbreviated MRI has high value of sensitivity for elucidation of axillary adenopathy and NAC invasion. In a prior study, MIP as a part of abbreviated protocol, was applied for excluding

Table 2
Comparative results of abbreviated and standard protocols.

	Abbreviated	standard
Main mass detection	52 (96.3)	52 (96.3)
Main mass size	38.6 ± 17.3	40.7 ± 17.9
Mass extent		
Unicentric	22 (40.7)	21 (38.9)
Multifocal	20 (30.7)	20 (37.0)
Multicenter	10 (18.5)	11 (20.4)
None	2 (3.7)	2 (3.7)
NME presence	45 (83.3)	46 (87.0)
Axillary LAPs		
Negative	4 (7.4)	5 (9.3)
Suspicious/positive	50 (92.6)	49 (90.7)
Nipple areolar complex involvement		
Negative	25 (46.3)	22 (40.7)
Suspicious/positive	29 (53.7)	32 (59.3)

Table 3
Concordance and discordance results of abbreviated and standard full protocols regarding evaluated imaging characteristics.

Features	concordance	discordance
Main Mass Detection	54 (100)	0 (0)
Main Mass size	49 (90.7)	5 (9.3)
Multifocal/multicenter status	53 (98.1)	1 (1.9)
NME	51 (94.4)	3 (5.6)
Axillary LAPs	51 (94.4)	3 (5.6)
Nipple areolar complex involvement	51 (94.4)	3 (5.6)

Table 4
Diagnostic performance of Abbreviated protocol in comparison to standard full protocol.

Characteristics	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Main Mass detection	100	100	100	100	100
Main mass size	90.6	100	100	16.7	90.7
Mass extent	98.1	100	100	50	98.1
NME	88.2	66.7	97.8	25	87
Axillary LAPs	97.9	60	96	75	94.4
Nipple areolar complex involvement	93.7	95.4	96.8	91.3	94.4

NAC involvement [23]. They concluded that NPV of MIP images for excluding occult NAC involvement was 99.5%. In the current study, NPV for NAC invasion was 91.3%. Given these results, the abbreviated protocol may be a reliable modality for evaluating/excluding the NAC involvement as a major component of the disease extent. Concerning the axillary adenopathy, we obtained higher sensitivity and lower specificity compared to what Le-felker et al. [21] found with 78% sensitivity and 90% specificity. This discrepancy may be due to different study population, because we include only subjects who were candidates for neoadjuvant chemotherapy, but in the aforesaid study, heterogeneous groups of patients with newly-diagnosed cancer were included.

Regarding to the fact that our investigated subjects did not include lobular carcinoma, and were almost all stage III or IV breast cancers with high aggressive nature, our abbreviated protocol was sufficiently capable of detecting cancer complications in comparison with the full protocol MRI. Generally, its accepted that performing breast MRI is not an essential step for evaluation of stage II or I breast cancers. On the other hand, considering less aggressive nature of the aforesaid tumors, its potentially likely that they don't show enhancement in the first two post-contrast phases. As so, the feasibility of using our abbreviated protocol for all breast cancers, including stage I and II, is under question and requires more studies to be answered.

Some study limitations warrant mention. First, abbreviated protocol was constructed by extracting relevant images from standard protocol and then interpret in a separate session due to the retrospective nature of the study. So, the recall bias may influence soundness of the results. While believing this inherent drawback was rationally reduced by interval time for the image analysis mentioned above, it is plausible that further works should investigate staging by the abbreviated protocol prospectively. Second, this investigation was conducted in referral center and expert fellowship-trained breast radiologists participated in imaging interpretation, so general applicability of the results in evaluation of the disease extent needs to be more confirmed in multicenter large-scale study with involving breast-dedicated and general radiologists.

Lastly, one of the greatest challenges in utilizing abbreviated MRI is the lack of standardization. The applied protocols of abbreviated MRI in breast imaging vary in different studies. As previously mentioned, in the current study we used "T1 fat saturated pre-contrast and the two first post-contrast sequences" as our protocol for abbreviated MRI. The first abbreviated protocol was proposed by Kuhl et al. consisting of one unenhanced acquisition, one contrast-enhanced acquisition, subtraction images, and maximum-intensity-projection (MIP) images. Thereafter, various protocols have been investigated by Kuhl et. al, and others, some of which include: "T1-weighted gradient-echo images before and then immediately after contrast medium injection", "axial gradient-echo dynamic series before and four times after contrast medium injection associated with an axial T2-weighted fast spin-echo sequence". Therefore, we suggest the conduction of studies focusing on determining standardized abbreviated protocol.

6. Conclusion

In this study, we have depicted detection ability of the abbreviated protocol equaled standard protocol in terms of identifying main mass. Furthermore, nearly all multifocal and multicentric breast cancers were detected by this protocol compared to standard breast MRI. Additionally, other components of disease extent such as NAC invasion, were appropriately evaluated by the abbreviated protocol. If confirmed in further prospective studies, our results can support the implementation of abbreviated MRI for assessing extent of disease. Hence, abbreviated protocols may serve as a suitable surrogate for standard protocol with significantly longer duration of acquisition and interpretation.

Ethics approval and consent to participate

We confirm that all experimental protocols were approved by Tehran University of Medical sciences. We confirm that all methods were carried out in accordance with relevant guidelines and regulations.

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CRediT authorship contribution statement

Ghazanfari Hashemi Mohamad: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Data curation, Conceptualization. **Talebi Vahid:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Conceptualization. **Arian Arvin:** Validation, Supervision, Resources, Project administration, Methodology, Conceptualization. **Sadighi Nahid:** Methodology, Data curation, Conceptualization. **Ahmadinejad Nasrin:** Visualization, Validation, Project administration, Methodology, Data curation, Conceptualization. **Eslami Bita:** Methodology, Formal analysis, Data curation.

Declaration of Competing Interest

The authors declare that they have no competing interests.

Data Availability

All of the data generated and analyzed during this study are included in our manuscript.

Acknowledgment

Not applicable.

Consent for publication

Not relevant.

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