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A preliminary study of the combination of ultrafast and abbreviated dynamic contrast

Enhanced breast magnetic resonance imaging

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Abstract

We combined the abbreviated and ultrafast magnetic resonance imaging (MRI) technique with the standard MRI protocol and compared lesion characterization quantitatively and qualitatively to the standard MRI protocol.

Fifty-six patients with breast cancer who underwent MRI from June 2017 to May 2018 and fulfilled our inclusion criteria were included. Three radiologists measured the lesion sizes, described the MRI findings using BI-RADS lexicon, and demarcated the regions of interest to extract the volumetric quantitative and semi-quantitative parameters. We used Pearson's correlation analysis comparing the quantitative and semi-quantitative parameters. To evaluate the inter-observer variability, we calculated the intra-correlation coefficient (ICC). We also analysed the correlation in BI-RADS lexicon.

There were 45 (80.4%) luminal and 11 (19.6%) non-luminal breast cancers, and the most common tumour subtype was invasive carcinoma (n = 48, 85.7%), followed by ductal carcinoma *in situ* (n = 8, 14.3%). Regarding correlation between the quantitative and semi-quantitative parameters, K^{trans} significantly correlated with the wash-in factor (r, 0.862; $P < .001$) and AUC value (r, 0.951; $P < .001$). The lesion size measured by standard and combined abbreviated-ultrafast phases and that from the surgical pathological specimens showed moderate agreement (ICC range, 0.516–0.578). The ICCs among the 3 readers were excellent for lesion size measurement, BI-RADS lexicon regarding lesion type, mass shape, margin, internal enhancement, non-mass enhancement distribution, and internal enhancement by the standard and combined abbreviated-ultrafast protocols.

The use of the modified and combined abbreviated-ultrafast MRI protocol provides a reliable measurement of the quantitative parameters and may aid in the screening of breast cancer.

Abbreviations: DCE = dynamic contrast-enhanced, MRI = magnetic resonance imaging.

Keywords: abbreviated magnetic resonance imaging protocol, ultrafast magnetic resonance imaging protocol, breast cancer screening, dynamic contrast-enhanced breast magnetic resonance imaging

1. Introduction

Magnetic resonance imaging (MRI) of the breast is well known as the most sensitive imaging tool (sensitivity, 66.7%–99.6%) for the detection of breast cancer along with its characterization by the use of contrast agents.[1–5] Breast MRI screening detects breast cancer at early stages and reduces the incidence of interval cancers. In addition, it is suggested that breast MRI screening improves the prognosis of women at increased risk of breast cancer.[6,7] However, because of the long scan time and high cost involved, the use of breast MRI has been limited only in high-risk women for screening purposes. To overcome this issues, abbreviated and ultrafast MRI protocols have emerged as more simplified and shortened MRI techniques with excellent diagnostic performance. Kuhl, et al[6] reported that cancer detection and diagnostic accuracy were not significantly different between the abbreviated protocol and the conventional dynamic contrast enhanced (DCE)-protocol. Furthermore, the specificity (94.3% vs 93.9%) and positive predictive value (24.4% vs 23.4%) were similar between the abbreviated and conventional DCE-protocol and the negative predictive value of the abbreviated protocol remains high (99.8%). However, because the acquisition time of abbreviated MRI is usually about 3 min, it does not provide the full dynamic information required for more precise tumour characterization and diagnosis.[6,8] Meanwhile, the ultrafast MRI utilises kinetic information of the very early phase within 90 s (20 phases) with at least 4.5 s/phase.[8–12]

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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A previous study[11] has reported that the ultrafast protocols were useful for distinguishing the benign from the malignant lesions. In the study,[11] there was a statistically significant difference between the benign and malignant lesions in terms of enhancement rate and kinetic AUC in the ultrafast imaging, and it was comparable to that of the standard kinetic assessment involving a shorter acquisition time. But due to the omission of the delayed phases, the morphological characteristics and even ductal carcinoma in situ (DCIS) might not be exactly assessed.

We hypothesised that abbreviated protocol allowing morphological assessment and ultrafast protocol providing kinetic information can play complementary roles. Thus, we combined the abbreviated and ultrafast protocols with shorter acquisition time and compared its diagnostic yield through the lesion characterization quantitatively and qualitatively to the standard DCE-protocol. To the best of our knowledge, several studies were conducted with these two protocols separately. However, the benefits of the combined technique for characterization of breast cancer were not evaluated.

2. Material and methods

2.1. Study population

This retrospective study was approved by the institutional review board. The requirement to obtain informed consent was waived. One-hundred and seventy-one patients with breast cancer were who underwent MRI from June 2017 to May 2018 were identified. After excluding patients who received neoadjuvant chemotherapy (n=29), who underwent MRI for postoperative surveillance (n=50), who underwent mammoplasty (n=3), or with insufficient clinical and pathological information (n=33), a total of 56 patients (mean age 51.8 years, range, 35−80) (Fig. 1) were included.

2.2. Imaging technique

DCE MRI was performed by a 3 T scanner (Skyra, Siemens AG, Erlangen, Germany) using a dedicated 18-channel phased-array breast coil. Bilateral breast MRI was performed using an axial T2 SPACE CAIPIRINHA sequence [TR/TE, 1200/98 msec; flip angle, 115°; thickness, 1 mm without an inter-slice gap; field of view (FOV), $350 \times 350\,mm^2$; matrix size, $1.1 \times 1.1 \times 1.0\,mm^3$; acquisition time, 4 min 12 s] and a 3D T1-weighted TWIST VIBE Dixon sequence (TR, 5.37 ms; TE, 3.69 msec; flip angle, 12°; matrix size, $1.0 \times 1.0 \times 1.0\,mm^3$; thickness, 1 mm without an inter-slice gap; FOV, $360 \times 358\,mm^2$). The contrast dynamic TWIST VIBE Dixon sequence was composed of 20 unenhanced phases with a total scan duration of 3 min. This was followed by the acquisition of 4 standard enhanced images and 3-dimensional data reconstructed using a TWIST view sharing. The TWIST view sharing was chosen as A=20% and B=20%, resulting in a temporal resolution of 8.1 second for the initial 20 phases except for the first 1 (22 s). The contrast medium (0.1 mL/kg body weight; Gadovist; Schering, Berlin, Germany) was injected with a flow rate of 1.5 mL/s, followed by a 30-mL saline flush.

2.3. Data analysis

All patients were reviewed by 3 dedicated breast radiologists (S. M.H., A.H.S., S.M.J., with 7, 9, and 1 year of clinical experience in breast imaging, respectively) in consensus. Each radiologist was blinded to the readings of the other radiologist during the initial review. When a discrepancy occurred, the radiologists reviewed the case together and reached a consensus. The breast MRI findings were described using terminologies from the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) 5th edition.[13] The regions of interest were demarcated within the tumour and volumetric quantitative and semi-quantitative parameters were extracted with nordicICE software (Bergen, Norway) applying the extended Tofts model.

The pathological data were reviewed, including the tumour type, size, histological grade, lymph node status, and immunohistochemistry findings. The molecular subtypes of breast cancer were categorised into the following 4 groups: hormone receptor-positive and HER2 (Human epidermal growth factor receptor 2)-negative (luminal A subtype), hormone receptor-positive and HER2-positive (luminal B subtype), hormone receptor-negative and HER2-positive (HER2 subtype), and hormone receptor-negative and HER2-negative (triple-negative subtype).

2.4. Statistical analyses

We used Pearson's correlation analysis for comparing the quantitative and semi-quantitative parameters [K^{trans} represent-

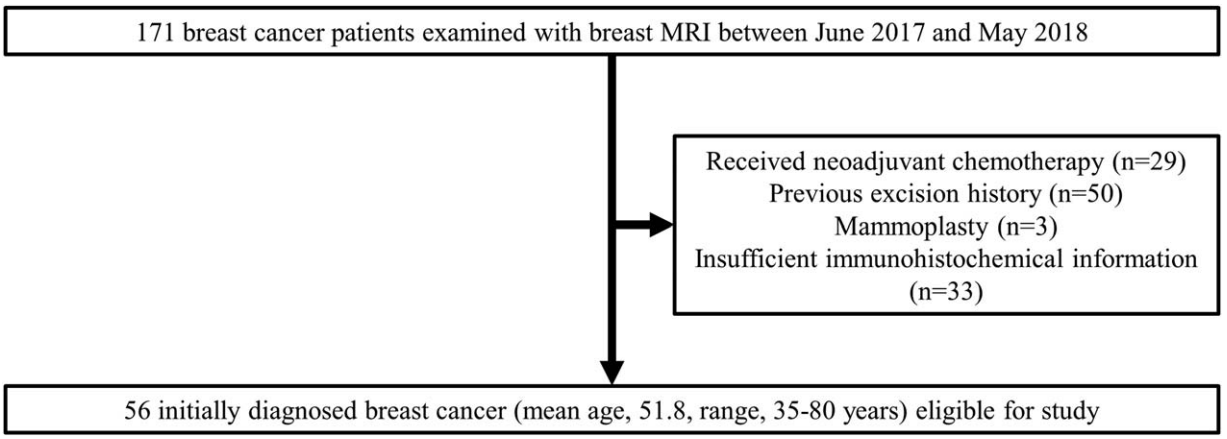

Figure 1. Flow chart of the study population.

Table 1

Quantitative parameters of the study population by tumour subtype.

		K^{trans}		Kep		Ve		AUC		Wash-in		Wash-out	
Tumour subtype	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Luminal type	45	0.39	0.20	0.98	0.34	85.64	39.36	188.98	80.00	0.04	0.02	0.03	0.02
Non-luminal type	11	0.51	0.33	1.09	0.42	91.36	34.71	238.87	143.90	0.04	0.02	0.03	0.02
P-value		0.25		0.37		0.66		0.29		0.29		0.77	
Invasive	48	0.44	0.24	1.03	0.34	87.06	39.15	207.16	98.29	0.04	0.02	0.03	0.02
DCIS	8	0.28	0.14	0.81	0.43	84.99	34.70	148.54	68.78	0.03	0.01	0.02	0.01
P-value		.07		.10		.89		.11		.37		.09	

Luminal type: Luminal A (ER positive or PR positive, HER2 negative) and Luminal B (ER positive or PR positive, HER2 positive)
AUC = area under the curve, DCIS = ductal carcinoma in situ, SD = standard deviation.

ing permeability as min^{-1}, Kep, reverse volume transfer constant, Ve, extravascular extracellular space volume per unit volume of tissue, area under the curve (AUC), and wash-in and wash-out values].[14] To evaluate the inter-observer variability, we calculated the intra-correlation coefficient (ICC) between the sizes measured by the 3 radiologists using the combined abbreviated-ultrafast and standard early enhancement phases and the sizes determined from the surgical pathological specimens. An ICC of $\leq$ 0.20 indicates slight agreement and 0.81−1.00 indicates almost perfect agreement. We also analysed Fleiss' kappa-value using R statistical software (version 3.3.3, R Foundation for Statistical Computing, Vienna, Austria) to find the correlation in BI-RADS lexicon for each lesion among the 3 radiologists. A *P*-value of $<.05$ was considered statistically significant. Statistical analyses were performed using SPSS software (version 23.0, Statistical Package for the Social Sciences, Chicago, IL).

3. Results

There were 45 (80.4%) luminal and 11 (19.6%) non-luminal breast cancers and the most common tumour subtype was invasive carcinoma (n = 48, 85.7%) followed by DCIS (n = 8, 14.3%). There were no statistically significant differences in the quantitative parameters (K^{trans}, Kep, and Ve) obtained from the combined abbreviated-ultrafast phase and semi-quantitative parameters (AUC, and wash-in and wash-out) obtained from the standard MRI phases according to the tumour subtypes, and invasive and DCIS (Table 1). Regarding the correlation between the quantitative and semi-quantitative parameters, K^{trans} significantly correlated with the wash-in factor (r, 0.862; $P < .001$), and AUC (r, 0.951; $P < .001$) (Table 2). The lesion size measured by standard and combined abbreviated-ultrafast phases and that from the surgical pathological specimens showed moderate agreement (ICC range, 0.516−0.578). There was a perfect agreement between the lesion size measured by the standard and combined abbreviated-ultrafast protocols (ICC, 0.867) (Table 3).

Table 2

Correlation between the quantitative and semi-quantitative parameters.

Quantitative parameter	Semi-quantitative parameter	*r*	*P*-value
K^{trans}	AUC	0.951	<.0001
K^{trans}	Wash-in	0.862	<.0001

r Pearson correlation analysis; AUC = area under the curve.

The ICC among the 3 readers were excellent for lesion size measurement, BI-RADS lexicon regarding lesion type, mass shape, margin, internal enhancement, non-mass enhancement distribution, and internal enhancement except kinetics (ICC, 0.236) using both standard and combined abbreviated-ultrafast protocols (Table 4, Fig. 2).

4. Discussion

Standard breast MRI is a sensitive imaging tool for breast cancer surveillance.[15] However, its use is limited to a screening tool because of high-cost, long scanning time, and a relatively lower specificity (72%).[16] With an increased frequency of breast cancer screening, in order to make breast MRI highly efficient and more accessible as a screening tool in average-risk women, some experts have appreciated the benefits of abbreviated breast MRI.[17–19] Abbreviated MRI consists of pre-contrast and 1 early post contrast T1 weighted series, post-contrast subtraction sequence, and subtraction reconstructed imaging data for interpretation. This simplified breast MRI protocol reduces the time for the examination, reduces the interpretation time for the radiologists, and reduces the overall cost, making it a more viable screening tool. Multiple studies have shown equivalent cancer detection rates, positive predictive value, and/or negative predictive value of this simplified breast MRI protocol as compared to that of the conventional MRI protocols.[6]

Though having comparable diagnostic accuracy, abbreviated MRI discards all dynamic information, and thus, may lower the specificity for characterization and diagnosis of the lesions. Meanwhile, ultrafast MRI has been investigated to acquire very early phase kinetic information and provide factors, such as time to enhancement to discriminate between benign and malignant breast lesions with high accuracy and specificity.[20] With our modified and combined abbreviated-ultrafast protocol, we could detect and characterise breast cancer quantitatively and qualita-

Table 3

Correlation between the size measurement by standard and combined abbreviated-ultrafast protocols.

Size variables		ICC
Standard	invasive	0.535
Standard	DCIS	0.574
Combined	invasive	0.516
Combined	DCIS	0.578
Standard	Combined	0.867

ICC = inter-observer variability.

Table 4

Image analysis correlation among the 3 readers.

Lesion characterization		Reader #1 Mean	Reader #1 SD	Reader #2 Mean	Reader #2 SD	Reader #3 Mean	Reader #3 SD	ICC
Size (mm)		24.02	15.01	25.77	18.65	25.70	17.82	0.84
Size (mm) ultrafast		22.18	13.67	23.95	16.27	24.18	16.28	0.869
		Reader #1		Reader #2		Reader #3		Fleiss' kappa
Lesion characterization		N	%	N	%	N	%	
MR BI-RADS (1–5)	3	3	5.36	6	10.71	5	8.93	0.768
	4	16	28.57	15	26.79	17	30.36	
	5	37	66.07	35	62.5	34	60.71	
Lesion type	Mass	41	73.21	40	71.43	40	71.43	0.775
	Non-mass	13	23.21	13	23.21	14	25	
	Mass and non-mass	2	3.57	3	5.36	2	3.57	
Mass shape	Not applicable	13	23.21	13	23.21	14	25	0.768
	Oval/round	16	28.57	10	17.86	8	14.29	
	Irregular	27	48.21	33	58.93	34	60.71	
Mass margin	Not applicable	13	23.21	13	23.21	14	25	0.775
	Circumscribed	18	32.14	11	19.64	10	17.86	
	Non-circumscribed	25	44.64	32	57.14	32	57.14	
Mass internal enhancement	Not applicable	13	23.21	15	26.79	17	30.36	0.684
	Homogeneous	8	14.29	10	17.86	10	17.86	
	Heterogeneous	27	48.21	22	39.29	19	33.93	
	Rim	8	14.29	8	14.29	8	14.29	
	Dark internal septation	0	0	1	1.79	2	3.57	
NME distribution	Not applicable	41	73.21	40	71.43	40	71.43	0.71
	Focal	0	0	2	3.57	1	1.79	
	Linear	4	7.14	1	1.79	0	0	
	Segmental	11	19.64	12	21.43	14	25	
	Regional	0	0	1	1.79	1	1.79	
NME internal enhancement	Not applicable	41	73.21	40	71.43	40	71.43	0.679
	Homogeneous	0	0	2	3.57	2	3.57	
	Heterogeneous	13	23.21	8	14.29	7	12.5	
	Clumped	2	3.57	6	10.71	7	12.5	
Kinetics	Type 1	4	7.14	2	3.57	3	5.36	0.236
	Type 2	19	33.93	32	57.14	45	80.36	
	Type 3	33	58.93	22	39.29	8	14.29	

ICC = interobserver variability, NME = non-mass enhancement, SD = standard deviation, Kinetics: Type 1 (persistent), Type 2 (plateau), Type 3 (wash-out).

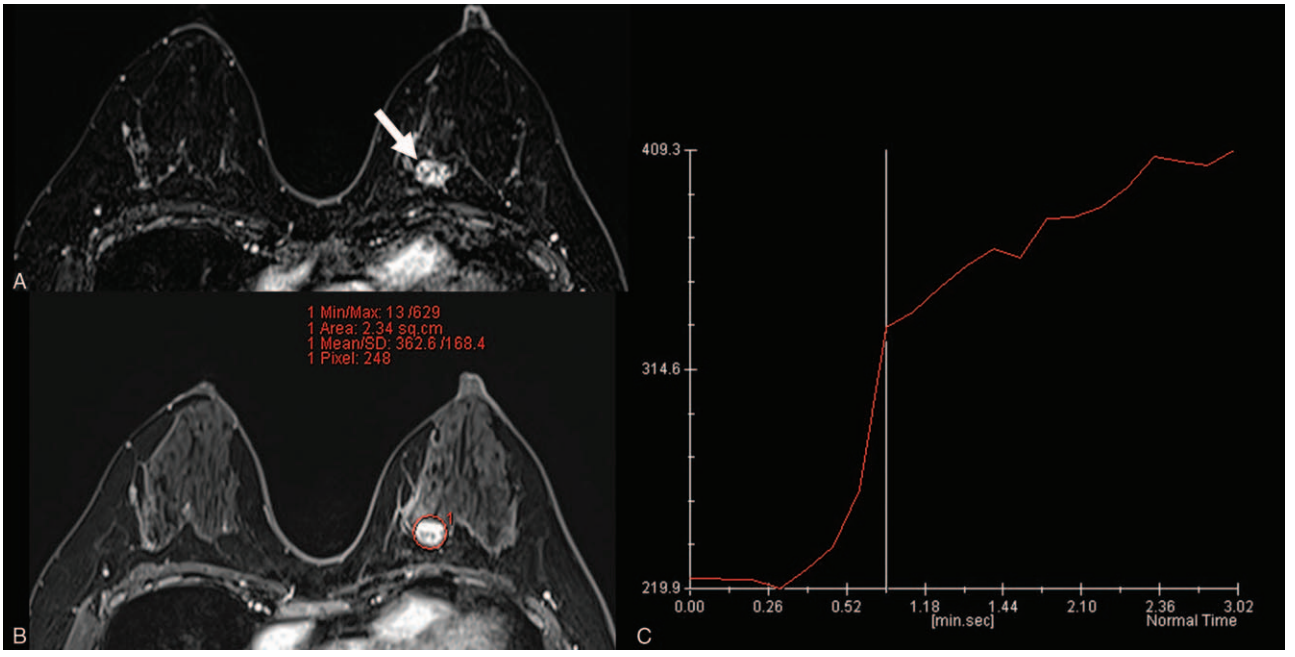

Figure 2. An invasive breast cancer in the left breast of a 49-year-old woman. (A) The combined abbreviated-ultrafast MRI phase using TWIST revealed an invasive breast cancer (showed by arrow). (B) The regions of interest were demarcated on the invasive cancer. (C) Relative enhancement vs. time curve derived from the combined abbreviated-ultrafast MRI phase using TWIST image.

tively. We used new ultrafast view sharing MRI sequences, such as time-resolved angiography with stochastic trajectories (TWIST), which could capture the images of the inflow of contrast agents at both high temporal and spatial resolutions.[21,22] This approach allows detection and classification of breast lesions with high accuracy based on the morphology and the maximum slope of the contrast enhancement over time curve. Further, the scan time is < 2 minute. In a previous study,[20] it was revealed that time to enhancement variable derived from ultrafast TWIST acquisitions allows the differentiation between malignant and benign breast lesions with high accuracy. We demonstrated a good correlation between quantitative and semi-quantitative parameters obtained from both the combined abbreviated-ultrafast and standard dynamic phases. Regarding size measurement, the inter-observer variability between the standard and combined abbreviated-ultrafast protocols showed a perfect agreement among the 3 radiologists. The size measurement was more accurate by the combined abbreviated-ultrafast phase with minor differences from the reference size of the surgical specimens. This may be due to more clearly demarcated tumour margins in the combined abbreviated-ultrafast protocol. We used TWIST acquisition which provides higher temporal and spatial resolution.[21,23] Although we did not specifically analyse the effects of the background parenchymal enhancement (BPE), it may be also due to less enhancement of BPE in very early acquired images. Indeed, BPE has a negative impact on the detection, diagnosis, and staging of breast cancer.[24] In addition, the inter-observer variability in characterizations of breast cancers according to the BI-RADS MRI lexicon showed an almost substantial agreement among the 3 radiologists, except for kinetics. We anticipate that this was because we did not use the commercially available CAD software. Our study results show that the modified combined abbreviated-ultrafast protocol has the potential to be used for screening of breast cancer with shorter examination time while maintaining lesion characterization.

There are several limitations to our study. First, this study was a retrospective 1 and conducted in a single tertiary referral centre. Further, this study involved a small number of cases with only breast cancer, and thus, we could not evaluate the diagnostic performance between the combined and standard protocols. However, this study was performed to reveal the preliminary results of the efficacy of combined abbreviated-ultrafast protocol in tumour characterization. By incorporating the abbreviated protocol within the standard MRI protocol, future studies could be conducted with the combined abbreviated-ultrafast MRI protocol for screening of breast cancer. Finally, the BIRADS assessment is in this study has very limited usefulness, because the radiologists knew that all of the lesions were malignant.

In conclusion, the use of modified and combined abbreviated-ultrafast MRI protocol provides a reliable measurement of the quantitative parameters for the screening of breast cancer. With more future prospective trials in a larger population, this novel technique comprising of the benefits of both abbreviated and ultrafast MRI protocols may serve a viable alternative to the standard full MRI protocol for breast cancer screening.

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