Multireader Study on the Diagnostic Accuracy of Ultrafast Breast Magnetic Resonance Imaging for Breast Cancer Screening

Jan C.M. van Zelst, MSc, MD, Suzan Vreemann, MSc,* Hans-Joerg Witt, MSc, PhD,† Albert Gubern-Merida, PhD,* Monique D. Dorrius, MD, PhD,‡ Katya Duvivier, MD,§ Susanne Lardenoije-Broker, MD,* Marc B.I. Lobbes, MD, PhD,|| Claudette Loo, MD, PhD,¶ Wouter Veldhuis, MD, PhD,# Jeroen Veltman, MD, PhD,** Daniel Drieling, MSc, PhD,† Nico Karssemeijer, PhD,* and Ritse M. Mann, MD, PhD**

Objectives: Breast cancer screening using magnetic resonance imaging (MRI) has limited accessibility due to high costs of breast MRI. Ultrafast dynamic contrast-enhanced breast MRI can be acquired within 2 minutes. We aimed to assess whether screening performance of breast radiologist using an ultrafast breast MRI-only screening protocol is as good as performance using a full multiparametric diagnostic MRI protocol (FDP).

Materials and Methods: The institutional review board approved this study, and waived the need for informed consent. Between January 2012 and June 2014, 1791 consecutive breast cancer screening examinations from 954 women with a lifetime risk of more than 20% were prospectively collected. All women were scanned using a 3 T protocol interleaving ultrafast breast MRI acquisitions in a full multiparametric diagnostic MRI protocol consisting of standard dynamic contrast-enhanced sequences, diffusion-weighted imaging, and T2-weighted imaging. Subsequently, a case set was created including all biopsied screen-detected lesions in this period (31 malignant and 54 benign) and 116 randomly selected normal cases with more than 2 years of follow-up. Prior examinations were included when available. Seven dedicated breast radiologists read all 201 examinations and 153 available priors once using the FDP and once using ultrafast breast MRI only in 2 counterbalanced and crossed-over reading sessions.

Results: For reading the FDP versus ultrafast breast MRI alone, sensitivity was 0.86 (95% confidence interval [CI], 0.81–0.90) versus 0.84 (95% CI, 0.78–0.88) (P = 0.50), specificity was 0.76 (95% CI, 0.74–0.79) versus 0.82 (95% CI, 0.79–0.84) (P = 0.002), positive predictive value was 0.40 (95% CI, 0.36–0.45) versus 0.45 (95% CI, 0.41–0.50) (P = 0.14), and area under the receiver operating characteristics curve was 0.89 (95% CI, 0.82–0.96) versus 0.89 (95% CI, 0.82–0.96) (P = 0.83). Ultrafast breast MRI reading was 22.8% faster than reading FDP (P < 0.001). Interreader agreement is significantly better for ultrafast breast MRI (κ = 0.730; 95% CI, 0.699–0.761) than for the FDP (κ = 0.665; 95% CI, 0.633–0.696).

Conclusions: Breast MRI screening using only an ultrafast breast MRI protocol is noninferior to screening with an FDP and may result in significantly higher screening specificity and shorter reading time.

Key Words: breast MRI, screening, breast cancer, ultrafast breast MRI, abbreviated breast MRI, multireader, multicase study

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Breast cancer prognosis is highly improved by early detection despite advances in therapeutic options that have been introduced over the past decades.[1] Screening for breast cancer is therefore one of the most effective methods to reduce breast cancer mortality.[2,3] Breast magnetic resonance imaging (MRI) has been shown to be the most accurate imaging modality for breast cancer screening in all risk groups[4,5] and is advised for all women with a lifetime risk (LTR) of more than 20% for the development of breast cancer.[6,7] However, in practice, its use is restricted due to uncertain cost-effectiveness of breast MRI in women without *BRCA* gene mutations and limited availability of MRI scanners.[8]

The high costs of breast MRI are mainly due to the costs of the examination itself.[9] A state-of-the-art multiparametric breast MRI protocol may take up to 20 minutes depending on the choice of MRI sequences and includes multiple conventional T1-weighted dynamic contrast-enhanced (DCE) sequences, a T2-weighted sequence, and diffusion-weighted imaging (DWI). Recently, abbreviated breast MRI protocols (AP) have been introduced, reducing the time needed for image acquisition and interpretation compared with the full diagnostic protocol (FDP) substantially. Although published series are small, the sensitivity of breast MRI for screening seems to be uncompromised,[10] although the frequency of probably benign lesions that require short-term follow-up increases. This might be due to the fact that all dynamic information is lost and lesion assessment is based upon morphology alone.

Ultrafast breast MRI sequences re-enable dynamic evaluation of contrast inflow during, and shortly after, contrast agent injection, while preserving a diagnostic spatial resolution that allows morphologic analysis of breast lesions. Time-resolved angiography with stochastic trajectories (TWIST) is such an ultrafast high spatial and high temporal resolution DCE-MRI sequence, allowing acquisition of 20 whole breast 3D volumes within 102 seconds (Fig. 1). In previous work, it was shown that the multiple volumes acquired allow assessment of dynamic parameters such as "maximum slope (MS)" and "time-to-enhancement (TTE)" with an excellent discriminating capacity between benign and malignant lesions.[11–13]

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From the *Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Nijmegen, the Netherlands; †MeVis Medical Solutions, Bremen, Germany; ‡Department of Radiology, University Medical Center, Groningen; §Department of Radiology, VU University Medical Center, Amsterdam; ||Department of Radiology and Nuclear Medicine, Maastricht University Medical Center, Maastricht; ¶Department of Radiology, the Netherlands Cancer Institute; #Department of Radiology, University Medical Center, Utrecht; and **Department of Radiology, ZGT Medical Center, Almelo, the Netherlands.

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Correspondence to: Ritse M. Mann, MD, PhD, Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Internal Route 766, Geert Grooteplein 10, 6525GA Nijmegen, the Netherlands. E-mail: Ritse.mann@radboudumc.nl; Jan C.M. van Zelst, MSc, MD, Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Internal Route 766, Geert Grooteplein 10, 6525GA Nijmegen, the Netherlands. E-mail: jan.vanzelst@radboudumc.nl.

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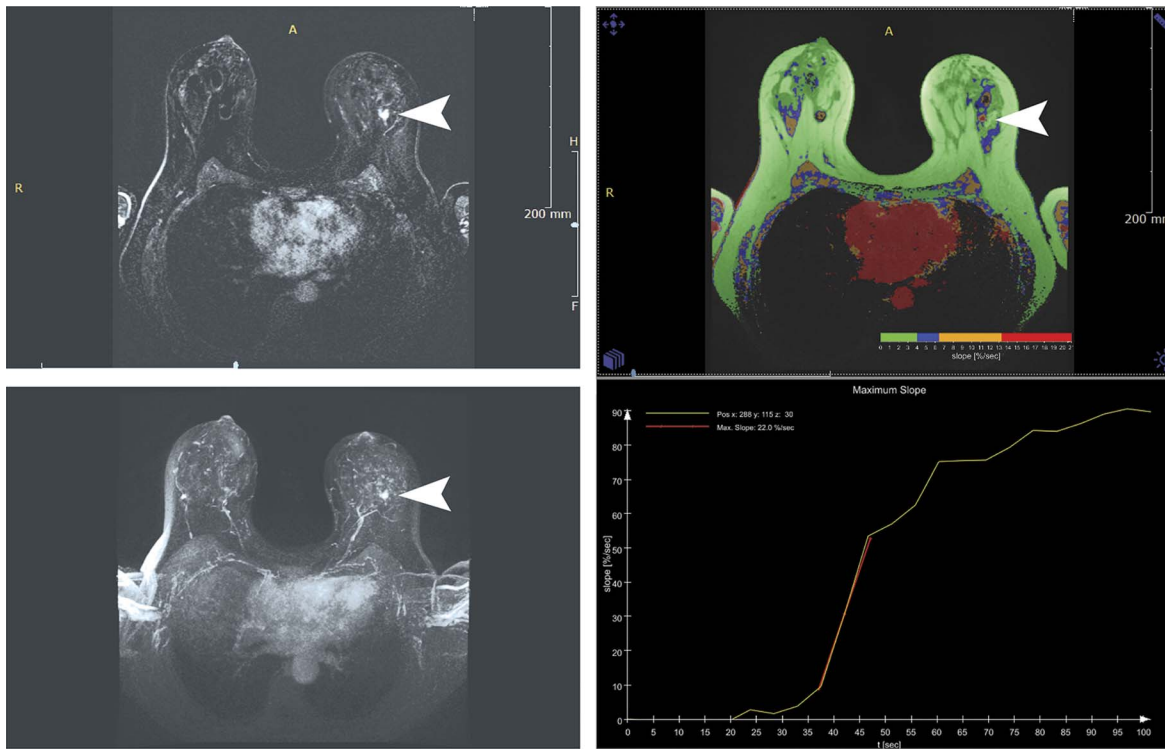

FIGURE 1. Screenshot of an ultrafast breast MRI hanging protocol. The left upper screen shows the subtraction image of the last acquisition. The left lower screen shows a maximum intensity projection of the same time point. Using the arrow keys toggling through the different time points is possible to determine TTE. In the right upper screen, MS is provided as a color-coded overlay on top of the native T1-weighted acquisition (colors correspond to the cutoffs presented in Mann et al[11]). The right lower screen shows the actual relative enhancement versus time curve during the wash-in of contrast at the position of the cursor, with the maximum slope presented as a red line. At the arrowheads, an 11-mm invasive lobular carcinoma is depicted. Morphology, the type 3 wash-in curve, and a maximum slope of 22.0%/s allow classification of this lesion as BI-RADS 4. In addition, TTE was 8.6 seconds (not shown), further pointing in the direction of the malignant nature of this lesion.

Although ultrafast breast MRI using TWIST has been shown to achieve higher diagnostic accuracy than conventional T1-weighted DCE-MRI for differentiation of known lesions, its use as a standalone technique for breast MRI screening remains to be evaluated. In this study, we offered a multiparametric breast MR screening protocol including TWIST to all women participating in our breast MRI screening program, to investigate the performance of dedicated breast radiologists using either the FDP or the ultrafast breast MRI protocol (UBMP; TWIST) for breast screening.

MATERIALS AND METHODS

We designed a multireader, multicase (MRMC) study using a prospectively acquired cohort of women at high risk who underwent a bitemporal breast MRI screening examination for routine clinical care. This protocol interleaves ultrafast breast MRI acquisitions just before and during contrast examination in the conventional DCE series, as described previously[11] (Fig. 2, Table 1). The study was approved by the institutional review board, and the need for informed consent was waived.

Study Subjects

Patient acquisition was performed in a single academic institution between January 2012 and June 2014. All women participating in the institution's intermediate- and high-risk screening program (LTR >20%) were scanned using the above described hybrid bitemporal breast cancer screening MRI protocol at 3 T (Skyra, or Magnetom trio; Siemens, Erlangen, Germany) that included, apart from TWIST and conventional DCE-MRI sequences (volume interpolated breath-hold examination), also a T2-weighted sequence and DWI. Details of the various sequences are given in Table 1 and Figure 2.

In total, 1791 screening breast MRI examinations were performed in 954 women with a screening indication during the inclusion period. A total of 1342 MRI scans were reported as Breast Imaging Reporting and Data System (BI-RADS) 1 or BI-RADS 2 and had at least 2 years of negative follow-up. These were regarded as normal. In 249 cases, the report was normal, but follow-up was shorter than 2 years. These were classified as uncertain. Thirty scans were reported as BI-RADS 3 and underwent short-term follow-up. Eighty-nine women were

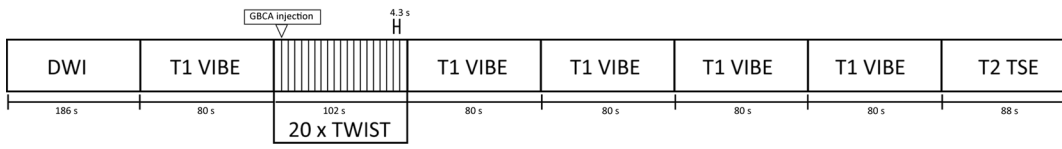

FIGURE 2. Schematic representation of the hybrid breast MRI screening protocol where 20 series of ultrafast breast MRI acquisitions (TWIST) are interleaved with the precontrast and first postcontrast VIBE acquisitions. The full hybrid protocol also consists of diffusion-weighted imaging and T2-weighted imaging. MRI, magnetic resonance imaging; TSE, turbo spin echo; TWIST, time-resolved angiography with stochastic trajectories; VIBE, volume interpolated breath-hold examination; DWI, diffusion-weighted imaging.

TABLE 1. Hybrid Bitemporal Breast Cancer Screening MRI Protocol

Breast MRI Screening Protocol				
	Ultrafast Breast MRI	**Full Diagnostic Protocol**		
	T1 (TWIST)	**T1 (VIBE)**	**DWI**	**T2 (TSE)**
Spatial resolution, mm	1.0 × 0.9 × 2.5	0.9 × 0.8 × 1.0	1.5 × 1.5 × 4.0	1.3 × 1.1 × 2.5
No. time points	20	5	1	1
Temporal resolution per time point	4.3 s	80 s	186 s	88 s
FOV	360	360	340	340
TE/TR, ms	2.02/3.96	1.71/5.50	60/6400	143/3220
FA	20	20	N/A	80
Parallel imaging factor (GRAPPA)	3	3	2	3
Reordering	Standard	3D centric	Standard	Standard
Central zone	15%	N/A	N/A	N/A
Sampling density outer zone	10%	N/A	N/A	N/A
Breast coil	AI breast coil (Siemens) 16 channels			
Contrast agent	Dotarem (Guerbet), 2.5 mL/s, 0.1 mmol/kg			
Power injector	Medrad, Warrendale, PA			

MRI indicates magnetic resonance imaging; TSE, turbo spin echo; TWIST, time-resolved angiography with stochastic trajectories; VIBE, volume interpolated breath-hold examination; DWI, diffusion-weighted imaging; FOV, field of view; TE/TR, echo time/repetition time; FA, flip angle; GRAPPA, generalized autocalibrating partial parallel acquisition; FDP, full diagnostic protocol; N/A, not applicable.

recalled for BI-RADS 4 or BI-RADS 5 findings and underwent a biopsy of the suspicious screen-detected breast abnormality (some more than once). In 34 women, cancer was detected, and in 55 women, the biopsy results showed a benign lesion. In 2 of the women with cancer, a second primary cancer was detected in a consecutive MRI examination within the study data range.

Generation of the Dataset for the MRMC Study

Figure 3 summarizes the selection procedure for cases that were included in the reader study. First, the MRI examinations that led to biopsy for 85 of the 89 biopsied women with MRI screen-detected (biopsied) abnormalities were included. For the women with more than 1 cancer, only the first cancer was included. The remaining 4 biopsied cases (3 malignant and 1 benign) were excluded because the hybrid MRI protocol was not completely performed.

Subsequently, 140 cases were randomly selected from all normal MRI examinations. Of the initially selected cases, 23 were thereafter also excluded because biopsies were performed based on MRI findings in a previous screening round. One further normal case was excluded based upon an incompletely scanned MRI protocol. Cases that were classified as uncertain and cases that were reported as BI-RADS 3 were excluded from the selection procedure.

Because in normal screening practice the prior examination will be available, we also collected MRI scans of approximately 1 year earlier for all selected cases, when available.

The final dataset therefore consisted of 201 cases with 153 prior examinations, including 31 malignant cases with 18 prior examinations, 54 benign cases with 25 prior examinations, and 116 normal cases with 110 prior examinations. All MRI scans were split into an FDP with an acquisition time of 13 minutes, and a UBMP with an acquisition time of 1 minute and 42 seconds (Table 1).

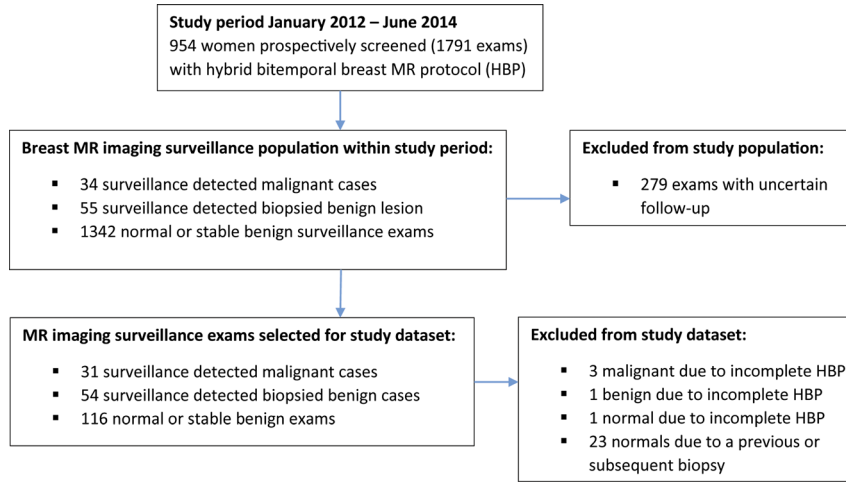

FIGURE 3. Flow diagram of the case collection and selection procedure. MR, magnetic resonance; HBP, hybrid bitemporal protocol; BI-RADS, Breast Imaging Reporting and Data System.

Study Readers

Seven dedicated breast radiologists were recruited from 7 expert centers throughout the Netherlands. All readers were experienced in the evaluation of both ultrafast breast MRI and full diagnostic protocols, because all readers are also involved in the Dutch nationwide DENSE trail in which similar hybrid protocols are mandatory.[14] We also provided them with a handout of the previously determined cutoffs for MS and TTE.[12,13] Breast MRI experience for the participating radiologists in our study was 6 to 15 years.

The Reader Study

The MRMC study had a crossover and counterbalanced design. Each breast radiologist read all cases twice. The readings were performed in 2 separate 1-day reading sessions with at least 4 weeks in between (mean, 4.4 weeks; range, 4–6 weeks). In each reading session, 201 breast MRI examinations (and priors when available) were read, 50% of cases using the FDP and 50% of cases using only ultrafast breast MRI. A case was never read twice in 1 reading session. Per reading session, we randomized the order of cases and the order of the screening protocol for each reader.

Reading Methodology

Fixed breast MRI screening workflows were designed for both the FDP and the UBMP and implemented into a dedicated breast MRI screening workstation that was created specifically for the purpose of this study (MeVis Medical Solutions, Bremen, Germany). In these workflows, mandatory steps needed to be completed to ensure that all sequences available in both screening protocols were evaluated (Appendix Figures 1 and 2, Supplemental Digital Content, http://links.lww.com/RLI/A393).

For each case, the age of the patient and the reason for the screening examination was provided to the radiologists. No other clinical information was given.

After each step in the reading protocol, readers were asked to rate whether the case was normal or abnormal and to provide a level-of-suspiciousness score on a scale from 0 to 100. After the final step, a BI-RADS score needed to be assigned on top of this assessment. The radiologists were allowed to give a BI-RADS 0 score to cases that they felt were of insufficient diagnostic quality. The scoring methodology was applied to both FDP and ultrafast breast MRI reading.

Statistical Analysis

Cases scored by any reader as BI-RADS 0 in the final assessment were considered as missing data and excluded from analysis.

Cases scored BI-RADS 3 or higher were considered positive. Sensitivity, specificity, and positive predictive value (PPV) were calculated for readings of individual readers and compared using McNemar test. Generalized estimation equation (GEE) analyses were used to compare pooled data corrected for repeated measurements by multiple readers.

Based upon the level-of-suspiciousness scores, MRMC receiver operating characteristics (ROC) analysis was performed to determine and compare the area under the ROC curve (AUC) of the FDP and ultrafast breast MRI readings for the individual radiologists and for the pooled data using dedicated statistical MRMC-ROC software (JAFROC v. 4.2.1) that uses analysis of variance and jackknifing cross-validation.[15,16] Pooled results were calculated using a random effect for both readers and cases. The study had a power of 0.83 to detect a 5% absolute decrease in the AUC.

Independent sample *t* tests were used to compare the reading time (RT) individual radiologists needed for FDP examinations and ultrafast breast MRI examinations. Bootstrapping was performed with 1000 samples to determine the 95% confidence intervals. Pooled RT needed for screening FDP and ultrafast breast MRI examinations was compared using GEE.

Fleiss kappa was used to compute interobserver agreement for dichotomised BI-RADS scores (BI-RADS 1 and 2: negative; BI-RADS 3, 4, and 5: positive). Fleiss kappa can be interpreted using Landis and Koch definition[17]: 0–0.20 as 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.

All statistical analysis except for the ROC analyses and GEE were performed in SPSS 20.0 (IBM statistics, Armonk, NY). Multireader, multicase ROC analysis was performed using JAFROC v.4.2.1. Generalized estimation equation was performed using R (R foundation for statistical computing, Vienna, Austria) using the package "geepack."

RESULTS

Patient Characteristics and Image Quality

Table 2 summarizes the characteristics of the included cancers and benign lesions. Mean age of women diagnosed with breast cancer was 45.8 years (SD, 10.5; range, 31–74), of women with benign lesions, 37.5 years (SD, 9.7; range, 20–55), and of women with a normal examination, 44.3 years (SD, 10.9; range, 24–69). Seventy-five women were known *BRCA1* mutation carriers, 55 *BRCA2* mutation carriers, 4 *PTEN* mutation carriers, 14 underwent radiation therapy to the chest at a young age, 33 had a strong family history, 15 had a personal history of breast cancer below the age of 50 years, and 5 had other risk factors such as the use of hormone replacement therapy and high-risk lesions such as lobular carcinoma in situ. Ten cancers were seen in *BRCA1* mutation carriers, 10 in *BRCA2* mutation carriers, 3 in women with a strong family history, 4 in women with a personal history of breast cancer, 1 in a woman with a *PTEN* mutation, and 3 in women with other risk factors. In 11 cases, 1 or more radiologist(s) rated the image quality as insufficient for a screening examination either in the FDP (n = 9) or in the ultrafast breast MRI data (n = 2). These cases were not assigned a final assessment and therefore excluded from analysis.

Screening Performance

Table 3 summarizes the screening performance. Pooled sensitivity of all radiologists was equal for ultrafast breast MRI and the FDP (0.84; 95% CI, 0.78–0.88 vs 0.86; 95% CI, 0.81–0.90, respectively; $P = 0.50$). Three of 7 radiologists had a slightly higher sensitivity reading ultrafast breast MRI than reading the FDP data, whereas this was the other way around for the other 4 radiologists.

Specificity of ultrafast breast MRI was higher than the FDP for all radiologists individually and significantly higher when pooled over all breast radiologists (0.82; 95% CI, 0.79–0.84 vs 0.76; 95% CI, 0.74–0.79, respectively; $P = 0.002$). The PPV was higher in 6 of 7 radiologists reading ultrafast breast MRI and also slightly higher when pooled (0.45; 95% CI, 0.41–0.50 vs 0.40; 95% CI, 0.36–0.45), but not statistically significant ($P = 0.14$).

Based upon the level-of-suspiciousness scores, the pooled AUC of all radiologists screening with ultrafast breast MRI alone was almost identical to that of screening with FDP (0.89; 95% CI, 0.82–0.96 vs 0.89; 95% CI, 0.82–0.96, respectively; $P = 0.83$; Fig. 4).

Reading Time

On average, breast radiologists needed 89.7 seconds (95% CI, 85.7–93.8; range, 19–262 seconds) to complete an FDP screening examination, compared with 69.2 seconds (95% CI, 66.3–72.1; range, 16–262 seconds) ($P < 0.001$) for an ultrafast screening examination (Table 4; Fig. 5). Six of 7 breast radiologists needed significantly less time to complete the ultrafast breast MRI examinations compared with the FDP examinations (range, 18.0%–38.6%). The highest reduction in

TABLE 2. Characteristics of the Histopathologically Proven Malignant and Benign Lesions Detected During the Study Period

Malignant cases (n = 31)	
Invasive ductal carcinoma (n = 21)	
Median size (SD)	11.0 (16.4)
TN stage	n
T1	15
T2	5
T3	1
N0	15
N1	6
Grade	n
I	1
II	6
III	12
Not available	2
Invasive lobular carcinoma (n = 3)	
Median size (SD)	11.0 (10.0)
TN stage	n
T1	2
T2	1
N0	2
N1	1
Grade	n
II	1
Not available	2
Ductal carcinoma in situ (pTis) (n = 5)	
Median size (SD)	10.0 (8.4)
Grade	n
II	3
III	2
Invasive tubular carcinoma (n = 1)	
Median size (SD)	7.0 (0.0)
TN stage	n
T1	1
N1	0
Grade	n
I	1
Invasive apocrine carcinoma (n = 1)	
Median size (SD)	9.0 (0.0)
TN stage	n
T1	1
N1	0
Grade	n
II	1
Benign cases (n = 54)	
Pathological diagnosis	Median size (SD)
Fibrosis/adenosis (n = 21)	10.0 (15.2)
Fibroadenoma (n = 16)	9.0 (5.5)
Cystic lesions (n = 4)	4.5 (0.6)
Normal breast tissue (n = 4)	6.5 (1.3)
Papilloma (n-3)	7.0 (6.4)
LCIS (n = 2)	5 (0.0)
Fat necrosis (n = 2)	7.5 (3.5)
Lymph node (n = 1)	5 (0.0)
Hamartoma (n = 1)	14 (0.0)

SD indicates standard deviation; TN, tumor and node stage according to TNM classification; pTis, pure ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

RT was observed in women with benign abnormalities (25.9 seconds/case, 24.9%, $P < 0.001$) followed by normal cases (19.0 seconds/case, 22.6%, $P < 0.001$). The decrease in RT in women with cancer was relatively modest (16.7 seconds/case, 19.2%, $P = 0.005$).

Interreader Agreement

Interreader agreement is substantial for both ultrafast breast MRI ($\kappa = 0.730$; 95% CI, 0.699–0.761) and the FDP ($\kappa = 0.665$; 95% CI, 0.633–0.696). However, based on nonoverlapping confidence intervals interreader agreement of ultrafast breast MRI is significantly better than for the FDP.

DISCUSSION

Our study shows that ultrafast breast MRI is an accurate alternative to the much lengthier full diagnostic protocols currently in use for breast cancer screening. Sensitivity between the 2 approaches was equal, and specificity for the ultrafast-only protocol was significantly higher than for the FDP. Noninferiority of the ultrafast breast MRI approach is also shown by the identical AUC for both approaches. In addition, the time breast radiologists needed to complete the UBMP was significantly shorter than the time needed for the FDP protocol, and a significantly better interreader agreement of the final assessment between radiologists was observed.

Using breast MRI as a tool for screening may be favored over mammography because of the significantly higher detection rate of breast cancers in women at average,[5] intermediate,[18] and high risk of developing breast cancer.[19–21] Current recommendations by the American Cancer Society, Society of Breast Imaging, and the European Society of Breast Imaging are to offer breast MRI screening to women with more than 20% LTR of developing breast cancer.[6,7,22] However, cost-effectiveness of breast MRI screening is only evident for women with an LTR more than 50% for the development of breast cancer, for example, *BRCA1* and *BRCA2* mutation carriers and women who received radiation therapy to the chest at an early age.[8,23,24] Hence, many national guidelines deviate from the international recommendations and reserve breast MRI screening for women in the highest-risk category. Further expansion of MRI screening to women with a slightly increased risk based on other genetic alterations, such as *CHEK2*, and women at average risk but with extremely dense breasts is therefore currently stalled, mainly for economic reasons.

The most important factor in modelling the cost-effectiveness of breast MRI screening is the high costs of the MRI examination itself.[9,25,26] Costs of a standard full diagnostic breast MRI protocol have been reported between US $250 to $619 for a 20- to 25-minute protocol.[8,24,27] Our results indicate that using TWIST as a single-sequence UBMP is at least as accurate as a lengthy FDP but requires only 2 minutes of magnet-time. A full examination can thus be performed in roughly 10 minutes including the time needed for patient positioning in the MR scanner. In addition, the time radiologists need to read an ultrafast MRI examination is significantly shorter than the time needed to read an FDP. In our study, the average RT of ultrafast breast MRI was 69.2 seconds, but this has been artificially prolonged by the fixed stepwise workflow and high prevalence of disease, which was evident to our readers. We expect that RT will be substantially shorter in real practice. In fact, in negative cases, evaluating the MIP generated from the UBMP images can be done in seconds. Therefore, the cost-effectiveness of accurate breast cancer screening with breast MR can substantially improve by using a UBMP.

Previous studies have shown that the use of "abbreviated MRI" may allow a similar gain in effectiveness of breast MRI as a screening tool. Kuhl et al[10] abbreviated a full diagnostic protocol to a 3-minute protocol consisting of a precontrast and postcontrast T1-weighted high spatial resolution sequence and evaluated the examinations using MIPs and subtracted contrast-enhanced T1 images. This abbreviated protocol

TABLE 3. Pooled and Individual Screening Performance for All Breast Radiologists

Reader	Screening Protocol	Sensitivity	95%CI Low to High	*P*	Specificity	95%CI Low to High	*P*	PPV	95%CI Low to High	*P*	Area Under the Curve	95%CI Low to High	*P*
Pooled	**FDP**	**0.86**	**0.81–0.90**		**0.76**	**0.74–0.79**		**0.40**	**0.36–0.45**		**0.89**	**0.82–0.96**	
	UBMP	**0.84**	**0.78–0.88**	**0.50**	**0.82**	**0.79–0.84**	**0.002**	**0.45**	**0.41–0.50**	**0.14**	**0.89**	**0.82–0.96**	**0.83**
1	FDP	0.83	0.70–0.97		0.68	0.61–0.75		0.33	0.22–0.45		0.85	0.75–0.95	
	UBMP	0.80	0.67–0.93	0.99	0.80	0.74–0.86	0.01	0.43	0.30–0.55	0.24	0.88	0.80–0.96	0.36
2	FDP	0.90	0.80–1.00		0.72	0.65–0.79		0.38	27.4–49.3		0.89	0.86–0.98	
	UBMP	0.93	0.83–1.00	0.99	0.77	0.70–0.84	0.31	0.42	0.30–0.55	0.65	0.92	0.81–0.97	0.26
3	FDP	0.90	0.77–1.00		0.71	0.64–0.78		0.37	0.26–0.47		0.91	0.84–0.99	
	UBMP	0.80	0.67–0.93	0.25	0.79	0.73–0.85	0.09	0.41	0.29–0.53	0.57	0.88	0.81–0.95	0.13
4	FDP	0.83	0.70–0.97		0.78	0.71–0.84		0.42	0.28–0.55		0.88	0.80–0.96	
	UBMP	0.87	0.73–0.97	0.99	0.81	0.75–0.87	0.49	0.46	0.32–0.59	0.60	0.88	0.80–0.96	0.96
5	FDP	0.83	0.70–0.97		0.83	0.78–0.89		0.48	0.35–0.61		0.89	0.81–0.96	
	UBMP	0.80	0.67–0.93	0.99	0.86	0.80–0.91	0.54	0.51	0.36–0.66	0.77	0.91	0.84–0.98	0.35
6	FDP	0.87	0.73–0.97		0.78	0.71–0.84		0.42	0.29–0.53		0.91	0.85–0.98	
	UBMP	0.90	0.77–1.00	0.99	0.82	0.76–0.88	0.33	0.48	0.36–0.61	0.49	0.89	0.81–0.97	0.50
7	FDP	0.87	0.73–0.97		0.83	0.76–0.88		0.49	0.34–0. 64		0.90	0.83–0.98	
	UBMP	0.77	0.60–0.90	0.25	0.85	0.79–0.91	0.54	0.48	0.35–0.61	0.94	0.89	0.82–0.97	0.76

Pooled results over all readers are given in boldface.

CI indicates confidence interval; PPV, positive predictive value; FDP, full diagnostic protocol; UBMP, ultrafast breast MRI protocol.

that abandoned all dynamic information showed noninferior sensitivity and specificity compared with the evaluation of the FDP that was acquired and was sequentially read. However, 37.7% of BI-RADS 3 ratings in the abbreviated protocol could be downgraded to BI-RADS 2 based upon the FDP.[10] Several subsequent studies have shown that the sensitivity of abbreviated breast MRI is comparable to an FDP at similar or slightly inferior specificity.[10,28–30] This underlines that the additional sequences in the FDP are mainly used for lesion classification and seem to be of limited value in a setting where most examinations are normal.

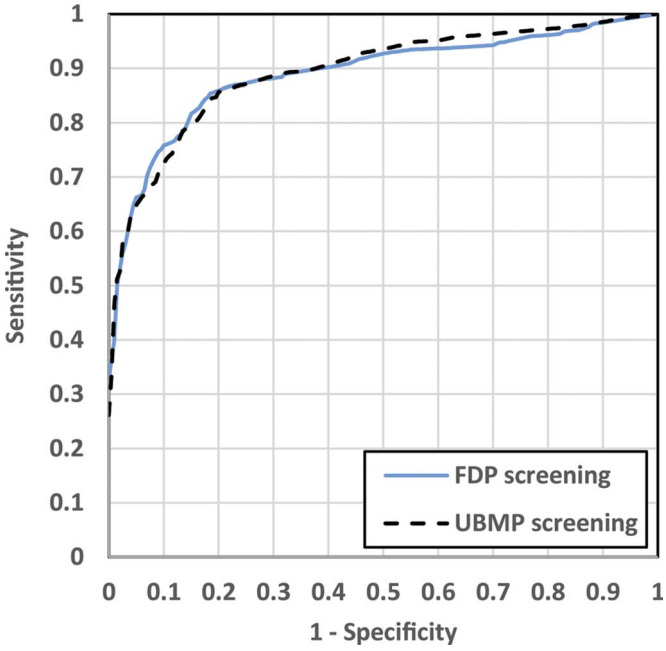

FIGURE 4. Pooled ROC curves for both ultrafast breast MRI (TWIST) and FDP reading. FDP, full diagnostic protocol; UBMP, ultrafast breast MRI protocol; TWIST, time-resolved angiography with stochastic trajectories.

However, the specificity of breast MRI is not trivial. False-positive findings are the most common harm of screening and lead to increased anxiety, unnecessary biopsies for benign lesions, and substantial costs of follow-up. Reports on early MRI screening trials showed specificities as low as 75% to 81%[4,31,32] and were therefore heavily criticized. Additional sequences such as T2-weighted imaging and DWI were added to most screening protocols to boost specificity. Although more recent studies show that the specificity of breast MR has improved substantially (range, 92%–97%),[5,18] it is unclear whether this is due to the use of these additional sequences, or due to improvements of the equipment and increased experience of radiologists in evaluating breast MRI. Regardless, and different from the results of the studies on abbreviated MRI without ultrafast dynamic imaging, in our study the specificity increased by the use of ultrafast breast MRI only as compared with the FDP, which underlines the value of the dynamic parameters obtained from ultrafast imaging for lesion differentiation. In clinical practice, this will lead to a small but relevant reduction of recalls for benign lesions, and thus limits the harms of screening.

It should be noted that the sensitivity of all our readers is below 100% for both ultrafast breast MRI and FDP evaluation, although readers were aware of the high rate of malignant findings in this study and hence likely more focussed to find all abnormalities than in clinical practice. Nonetheless, all the cancer cases included were screen-detected and therefore visible in the MRI scans. This underlines the difficulty of cancer detection in screening, as most of the lesions are subtle and can be easily overlooked or misinterpreted.[33] The development of computer-aided detection systems might be encouraged to prevent these overlook and interpretation errors.[13,34,35] Furthermore, double reading of cases might be advised, although this will obviously negatively affect cost-effectiveness.

Ultrafast breast MRI protocol still requires the administration of gadolinium-based contrast agents. A non–contrast-enhanced breast MRI techniques are promising alternatives for screening (eg, DWI and high spectral and spatial resolution MRI[36]); the diagnostic capacity of these sequences is currently not (yet) on par with those of contrast-enhanced imaging. Fortunately, the risks associated with gadolinium

TABLE 4. Reading Time for Both FDP and UBMP Reading

Reader	Reading Time FDP (s)	95% CI (low, high)		Reading Time UBMP (s)	95% CI (low, high)		Percentage Decrease	*P*
1	104.6	98.0	111.3	85.1	78.9	91.4	18.6	0.001
2	99.2	92.4	106.4	69.7	65.5	73.9	29.7	0.001
3	131.1	119.8	142.5	94.1	86.5	102.3	28.2	0.001
4	77.8	72.4	83.7	63.8	60.1	67.7	18.0	0.001
5	86.4	80.8	92.7	85.5	80.1	91.6	1.0	0.85
6	78.4	72.8	83.8	48.1	44.7	51.7	38.7	0.001
7	60.9	56.4	65.6	44.7	42.4	47.1	26.6	0.001
Pooled								
Average	89.7	85.7	93.8	69.2	66.3	72.1	22.8	<0.001
Normal	83.9	78.8	89.4	64.9	61.4	68.7	22.6	<0.001
Benign	103.9	98.1	110.1	78.0	72.5	84.0	24.9	<0.001
Malignant	86.8	76.9	97.9	70.1	64.0	76.7	19.2	0.005

Reading time was automatically recorded by the study's dedicated workstation.

CI indicates confidence interval; FDP, full diagnostic protocol; UBMP, ultrafast breast MRI protocol.

administration seem to be very low, especially for so-called macrocyclic contrast agents. In particular, there are no current clinical consequences of the documented deposition in the brain that particularly occurs with linear contrast agents.[37,38] Consequently, among others, the European Society of Breast Imaging currently still recommends the use of contrast-enhanced imaging for all breast MRI investigations that aim to detect cancer. It remains to be seen whether future developments in non–contrast-enhanced MRI will have the ability to render the use of contrast media obsolete.

Our study has limitations. The case-set created was enriched with consecutive breast MRI screening-detected malignant and benign lesions. We also excluded cases that were potentially ambiguous. Therefore, particularly the true specificity of screening cannot be assessed. However, the specificity of the clinical protocol was 95% (including BI-RADS 3 examinations as false-positives) and therefore well in line with recent literature. Because the ultrafast breast MRI acquisitions seem to be the most important parameter for the determination of specificity, the expected specificity of ultrafast MRI in screening is similarly high. It should be noted that we excluded cases scored as BI-RADS 0 by any of the readers from the analysis as they do not provide information on the diagnostic accuracy of the protocols. Furthermore, women older than 30 years also undergo full-field digital mammography as a complementary screening examination. This may affect the screening performance of the breast radiologists either positively or negatively. However, in this study, we did not include the mammograms and focussed on the value of MRI for screening alone. Nevertheless, according to recent reports, the added value of mammography in younger women at increased risk may be limited when MRI is available.[19,39,40]

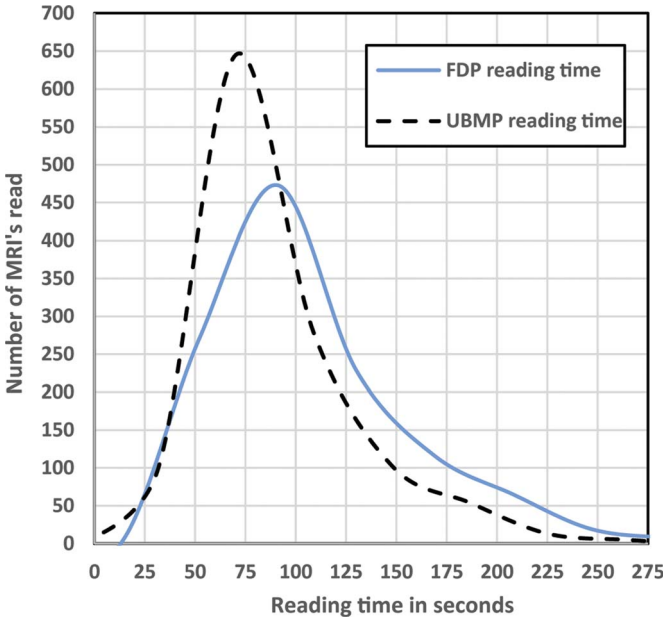

FIGURE 5. Pooled histograms for the time needed to complete both the ultrafast breast MRI (TWIST) and FDP examinations. FDP, full diagnostic protocol; ultrafast breast MRI protocol; TWIST, time-resolved angiography with stochastic trajectories.

In conclusion, ultrafast breast MRI using TWIST allows a bilateral whole breast dynamic MRI examination within 2 minutes and can be evaluated fast. Ultrafast breast MRI for breast cancer screening is noninferior to an FDP. In fact, ultrafast imaging may increase specificity in breast cancer screening. The use of ultrafast breast MRI may therefore facilitate cost-effective breast MRI screening in many more women than is achievable with FDPs currently in use.

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