Radiology

ORIGINAL RESEARCH • BREAST IMAGING

Multireader Diagnostic Accuracy of Abbreviated Breast MRI for Screening Women with Extremely Dense Breasts

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See also the editorial by Kataoka and Honda in this issue.

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Background: Abbreviated MRI may reduce costs and time of supplemental breast cancer screening. The Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial provides an opportunity to study this protocol in a true screening population.

Purpose: To compare multireader diagnostic accuracy of various abbreviated screening breast MRI protocols with that of the full multiparametric protocol in the DENSE trial, focusing on identifying the minimal protocol necessary to maintain high diagnostic accuracy.

Materials and Methods: In this secondary analysis of a subset from the DENSE trial, seven radiologists performed incremental readings of first-round screening MRI scans in women with extremely dense breasts and findings negative for cancer at mammography. Different sequences were added in four incremental steps. The first step included both high-temporal low-spatial and low-temporal high-spatial dynamic T1-weighted series, up to 120 seconds after contrast agent injection. The final step added all full-protocol sequences. Each radiologist assessed the same MRI scans and provided Breast Imaging Reporting and Data System scores for all four incremental steps. Pooled sensitivity and specificity were calculated across all readers per step using a generalized estimating equation model, and pooled reading time per step was calculated using a linear mixed model.

Results: The first-round screening included 518 MRI scans from 518 women (median age, 53 years; IQR, 51–59 years), including 83 breast cancers: 68 invasive cancers (82%) and 15 ductal carcinomas in situ (18%). There was no evidence of a difference in sensitivity between abbreviated protocol (84.3%; 95% CI: 77.7, 89.2) and the full multiparametric MRI protocol (85.9%; 95% CI: 80.0, 90.3; $P = .68$). There was also no evidence of a difference in specificity between abbreviated protocol (73.9%; 95% CI: 70.7, 76.9) and full protocol (75.8%; 95% CI: 72.8, 78.5; $P = .39$). The abbreviated protocol had a pooled reading time (49.7 seconds; 95% CI: 48.5, 50.9) that was almost 50% shorter than the full protocol (96.4 seconds; 95% CI: 94.3, 98.5; $P < .001$) with 70%–80% shorter scanning time, depending on hospital and scanner vendor.

Conclusion: In women in the DENSE trial with extremely dense breasts and findings that were negative for cancer at mammography, abbreviated breast MRI for first-round screening had high diagnostic accuracy that was comparable to full multiparametric protocol, at much shorter reading and scanning times.

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Supplemental material is available for this article.

Women with extremely dense breasts have a risk of breast cancer that is two- to sixfold higher than women with entirely fatty breasts and a 1.5- to twofold higher risk than women with average breast density (1–3). In addition, the sensitivity of mammography is limited among women with dense breasts (2,4,5). With full-field digital mammography, a program sensitivity of only 61% was observed based on biannual screening (2). Therefore, women with dense breasts may benefit from supplemental screening with more sensitive techniques.

The Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial examined the efficacy of supplemental MRI screening among asymptomatic women with extremely dense breasts (6). This trial showed that supplemental MRI screening lowered the interval cancer rate (7,8). Based on the results of the DENSE trial and other studies, the European Society of Breast Imaging and the American College of Radiology now recommend supplemental MRI screening for women with extremely dense breasts (9,10). Despite the proven benefits for women with dense breasts and despite proven cost-effectiveness in multiple scenarios, the widespread implementation of MRI screening has not yet been realized due to discussions about costs and capacity (11,12).

In the DENSE trial, all participants were scanned with a state-of-the-art 3-T multiparametric breast MRI protocol (6). Multiparametric scanning protocols are inherently lengthy (approximately 20 minutes). Moreover, many of the sequences are acquired for the purpose of lesion classification rather than lesion detection. In a screening setting, where most images show results that are negative for cancer, sequences aimed at lesion classification are often unnecessary. Therefore, the focus should be on reducing the breast MRI protocol to its absolute minimum in terms of both reading and scanning times while preserving sensitivity and positive predictive value (or keeping the rate of false-positive findings low). This approach minimizes the costs per MRI examination and maximizes MRI capacity.

Abbreviations

BI-RADS = Breast Imaging Reporting and Data System, DENSE = Dense Tissue and Early Breast Neoplasm Screening, GEE = generalized estimating equation

Summary

In women in the Dense Tissue and Early Breast Neoplasm Screening, or DENSE, trial with extremely dense breasts and findings that were negative for breast cancer at mammography, abbreviated breast MRI for first-round screening had high diagnostic accuracy comparable with the full multiparametric protocol with 50% shorter reading times and up to 80% shorter scanning times.

Key Results

- In a secondary analysis of 518 screening breast MRI examinations (83 breast cancers) from the Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial in women with extremely dense breasts and results negative for cancer at mammography, seven radiologists performed incremental readings, including highly abbreviated and full multiparametric protocol.
- Abbreviated and full MRI protocol had comparable sensitivity (84.3% vs 85.9%; $P = .68$) and specificity (73.9% vs 75.8%; $P = .39$).
- Abbreviated MRI had almost 50% shorter pooled reading time (49.7 vs 96.4 seconds; $P < .001$) and 70%–80% shorter scanning time.

Multiple previous studies, including those by Fischer et al (13) and Kuhl et al (14), have demonstrated that abbreviated MRI protocols can have diagnostic accuracy similar to that of a full multiparametric MRI protocol (13–21). Most of these previous studies compared the full multiparametric protocol with a single abbreviated MRI protocol. Moreover, protocols and study populations have been variable across studies of abbreviated MRI.

The full multiparametric MRI protocol of the DENSE trial provides an opportunity to study the accuracy of multiple, incremental abbreviated MRI protocols in a true screening population. Thus, in this study, the aim was to compare the multireader diagnostic accuracy of various abbreviated screening breast MRI protocols with that of the full multiparametric protocol in the DENSE trial, focusing on identifying the minimal protocol necessary to maintain high diagnostic accuracy.

Materials and Methods

On November 11, 2011, the trial was approved by the Dutch Minister of Health, Welfare, and Sport, under advisement from the Health Council of the Netherlands. All MRI trial participants provided written informed consent.

Study Design and DENSE Trial Participants

In this secondary analysis, a multireader multicase study was designed by using prospectively acquired breast MRI examinations from the DENSE trial, a randomized controlled trial embedded in the Dutch breast cancer screening program. The DENSE trial design and first results have been detailed elsewhere (6–8), and the study protocol can be accessed at ClinicalTrials.gov with identifier NCT01315015. Briefly, female participants (aged 49–75 years) with results that were negative for breast cancer at mammography (Breast Imaging Reporting and Data System [BI-RADS] score of 1 or 2) and extremely dense breasts (Volpara Density Grade 4, measured with Volpara software version 1.5; Volpara Health Technologies) were prerandomized to undergo either supplemental MRI screening (intervention arm) or mammography only (control arm, standard practice).

The MRI examinations included in this study were from DENSE trial participants and were therefore previously reported (7,8). The prior studies reported the initial results of the DENSE trial regarding supplemental full multiparametric MRI screening; this study reports results from abbreviated MRI protocols.

The final sample was composed of 518 MRI examinations from the first round of the DENSE trial. The results were normal (true-negative findings, 60% [310 of 518]), benign (false-positive findings, 24% [125 of 518]), or malignant (true-positive and false-negative findings, 16% [83 of 518]). The true-negative and false-positive findings were randomly sampled from all cases of true-negative and false-positive findings in the first round of the DENSE trial. The true-positive and false-negative findings were all available cases in the first round of the DENSE trial.

True-positive findings were breast cancers that were confirmed at histologic analysis and identified after a BI-RADS score of 3, 4, or 5 on MRI scans. False-negative findings (ie, interval cancers) were breast cancers that were diagnosed after findings that were negative for cancer on MRI scans before the next scheduled mammography examination. If no mammography was scheduled (eg, for women age >75 years), an interval cancer was defined as cancer diagnosed within 24 months after findings that were negative for cancer at MRI. False-positive findings were cases where no histologic analysis–confirmed breast cancer was present after a BI-RADS score of 3, 4, or 5 on MRI scans. True-negative findings were cases with findings that were negative for cancer on MRI scans (BI-RADS score of 1 or 2) that did not develop interval cancer.

Breast MRI Protocol

All MRI examinations were performed with 3-T systems using a dedicated bilateral breast coil. The macrocyclic gadolinium-based contrast agent gadobutrol (Gadovist; Bayer) (0.1 mmol per kilogram of body weight) was used. The full multiparametric MRI protocol in the DENSE trial allowed evaluation of various shortened protocols in a reader study by selectively presenting only parts of the acquired full multiparametric DENSE trial protocol. Different sequences were added incrementally in four steps, as follows: Step 1, dual high-temporal low-spatial and low-temporal high-spatial dynamic T1-weighted image series obtained right before and up to 120 seconds after contrast material injection only (Fig 1A); step 2, added diffusion-weighted imaging to the protocol (Fig 1B); step 3, added T2-weighted imaging (Fig 1C); and step 4, added all remaining sequences from the full multiparametric breast MRI protocol used in the DENSE trial (non–fat-saturated T1-weighted precontrast images, all remaining dynamic phases acquired after the first 120 seconds postcontrast, and enhancement curve kinetics) (Fig 1D).

Reading Procedure

Seven dedicated breast radiologists (R.M.M., K.D., M.D.F.d.J., P.K.d.K.D., C.E.L., J.V., and W.B.V., each with at least 16 years of experience reading breast MRI scans) participated in the reader study. All had participated in the DENSE trial. Each radiologist independently assessed the same set of MRI scans, each in a different randomized order. Each MRI scan was read by each radiologist, by following the four incremental steps. This method

was chosen because it most closely reflects the real-world situation, where the sequences from the shorter protocols are always available in the longer protocols. Radiologists were not aware of the number of true-positive findings, false-negative findings, true-negative findings, and false-positive findings in the dataset. Raw Digital Imaging and Communications in Medicine data have been used without postprocessing. Figure 2 shows the reading procedure.

The radiologists provided BI-RADS scores for each incremental step, determining the necessity for recall, based on the available data for that step. After completing a step, they proceeded to the next step for that case, repeating the process through to step 4. After step 4, the radiologists moved on to the next case. All steps were scored according to the BI-RADS (categories 1 [negative] to 5 [highly suggestive of breast cancer]). BI-RADS 0 was reserved for nondiagnostic images due to motion or other artifacts.

The readings (each examination read for each of the four incremental steps) were performed within a period of 2 or 3 consecutive days using dedicated high-throughput workstations, which recorded exact time stamps for the start and end of active reading and the entry of a BI-RADS score for each step.

Statistical Analysis

Images with BI-RADS scores of 1 or 2 were classified as negative for cancer (ie, no recall) and images with BI-RADS scores of 3, 4, or 5 as positive for cancer (ie, recall). For a sensitivity analysis, images with BI-RADS scores of 1, 2, or 3 were classified as negative results (no recall) and images with BI-RADS scores of 4 or 5 were classified as results that were positive for cancer (requiring recall for diagnostic workup). Reading steps scored as BI-RADS 0 were classified as missing data, and these measurements were therefore excluded from the analyses.

Sensitivity and specificity.—Sensitivities and specificities with 95% CIs per reader and per incremental step of MRI were first calculated by using a generalized linear model.

The pooled sensitivities of the seven readers per incremental step of MRI were calculated among the group of female participants with confirmed breast cancer. For this, a generalized estimating equation (GEE) model (geepack, RStudio; R Project for Statistical Computing) was used. The GEE model was created with the recall status as binary outcome and reading steps as covariate. The pooled sensitivities were calculated for all cases of breast cancer, including all invasive and ductal carcinoma in situ cases, as well as exclusively for cases of invasive breast cancer. A GEE model is a statistical method used to analyze correlated data, typically in situations where multiple measurements are taken on same subjects. Therefore, the GEE model was used to correct for the fact that the same images were read multiple times by the seven readers

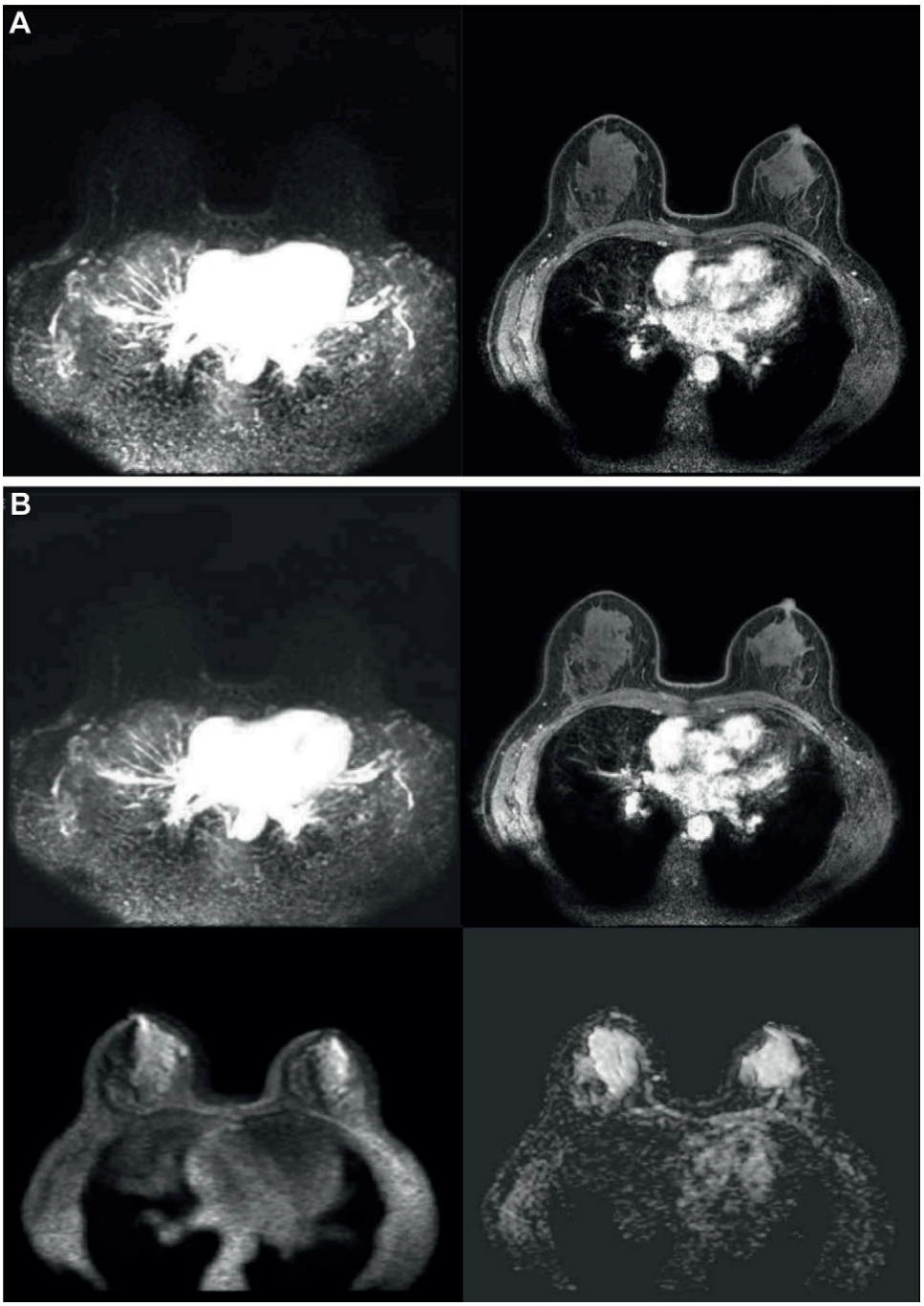

Figure 1: Axial images show the incremental steps 1–4. **(A)** Step 1: The first step consisted of the dual high-temporal low-spatial and low-temporal high-spatial dynamic T1 series, from before contrast material injection to 120 seconds after contrast injection only. **(B)** Step 2: The second step added diffusion-weighted images to the series available from step 1 *(Fig 1 continues).*

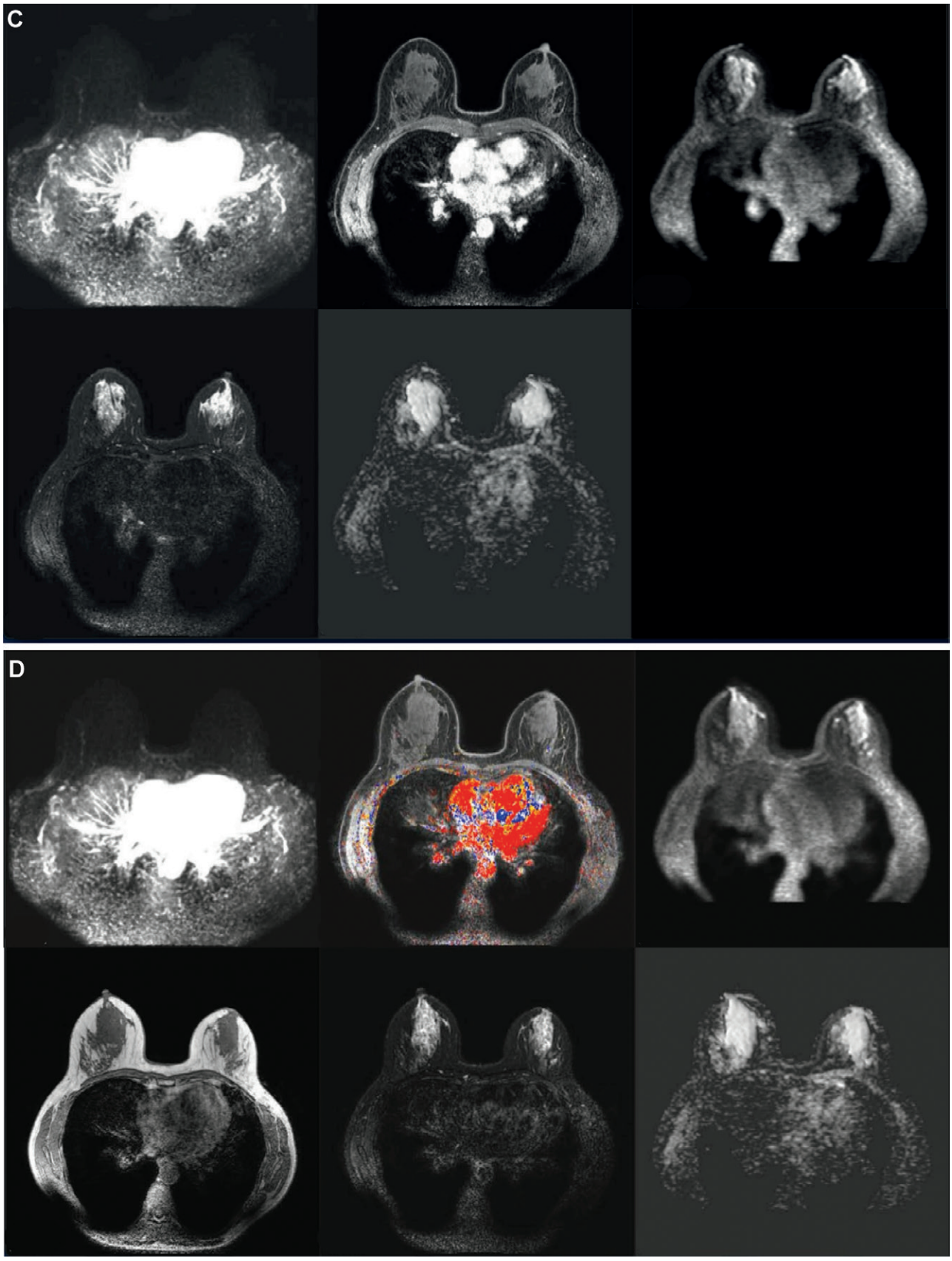

Figure 1 *(continued)*. (C) Step 3: The third step added T2-weighted images to the series available from steps 1 and 2. **(D)** Step 4: The fourth and final step added non–fat-saturated T1-weighted precontrast images, all remaining dynamic phases acquired after the first 120 seconds after contrast administration, and enhancement curve kinetics to the series available from steps 1, 2, and 3. This final step is the full multiparametric breast MRI protocol that was used in the Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial. The curve kinetics overlay is a colormap showing the standard three types of delayed curve kinetics: type-I kinetics, persistent increase (blue); type-II kinetics, plateau (yellow); and type-III kinetics, washout (red).

within each incremental step of MRI (22).

The pooled specificities of the seven readers were calculated among the participants without breast cancer, again using a GEE model. The sensitivities and specificities of the abbreviated MRI protocols (steps 1–3) were compared with those of the full-protocol MRI (step 4). Therefore, full-protocol MRI was used as the reference category.

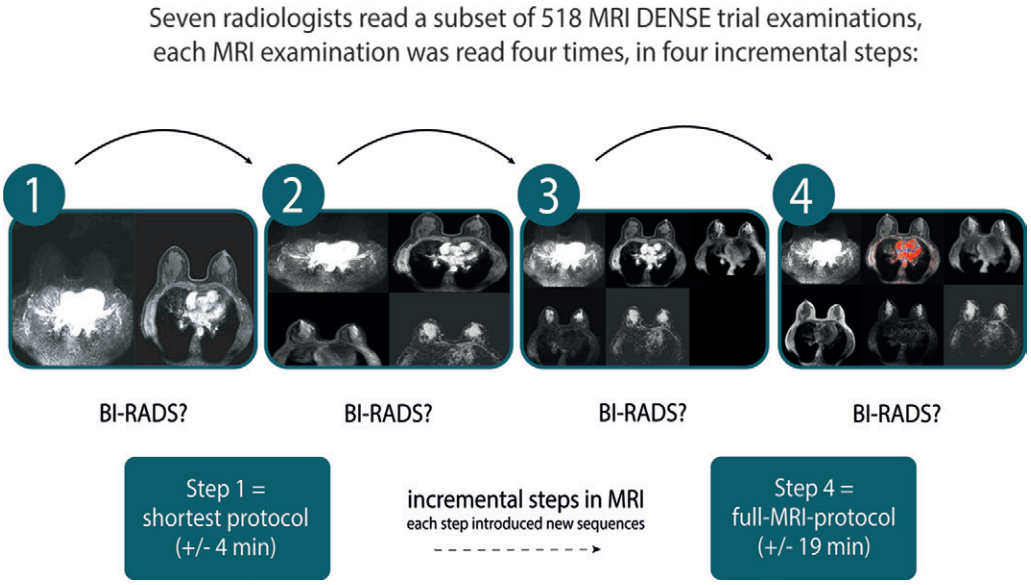

Figure 2: Schematic shows the reading procedure of this multireader, multicase study. Each radiologist assessed the same 518 MRI examinations in four incremental steps (steps 1–4), each step adding additional sequences to those from the preceding step. BI-RADS = Breast Imaging Reporting and Data System, DENSE = Dense Tissue and Early Breast Neoplasm Screening.

Reading time.—The available time stamps enable straightforward calculation of precise active reading time. The reading time for step 1 is the difference between the start-of-reading time stamp for that step and the time stamp for selection of BI-RADS score for that step. The active reading time for step 2 was calculated in an identical fashion to the preceding step: difference between the start-of-reading time stamp for step 2 and selection-of-BI-RADS-score time stamp for step 2. Because step 2 displays the same sequences that were just evaluated in step 1 with the addition of a diffusion-weighted sequence, the cumulative reading time for step 2 is the sum of the active reading time for step 1 and the active reading time for step 2. Similarly, the reading time for steps 3 and 4 was the sum of the reading time for that step and the previous steps. The average reading time (in seconds) per reader and per incremental step of MRI was first calculated by using a linear model. To calculate the pooled reading times per incremental step of MRI and corresponding 95% CIs, a GEE model was used. This model was used to correct for the fact that the same images were read multiple times by the seven readers within each incremental step of MRI.

Interobserver agreement.—The interobserver agreement was assessed by using the irr package in RStudio (R Project for Statistical Computing). The percentage of agreement on recall status was calculated (no recall: BI-RADS score, 1–2; recall: BI-RADS score, 3–5), and the Fleiss κ coefficient was calculated to assess the interobserver agreement for recall status. The Fleiss κ can be interpreted as follows: 0–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement. For sensitivity analysis, the agreement between the two readers who showed the highest level of concordance was examined.

All analysis was performed by using software (RStudio, version 4.2.2), and $P < .05$ was considered to indicate statistical significance.

Results

Participant Characteristics

In the first screening round of the DENSE trial, 4783 women underwent supplemental MRI screening. From the 4783 women, a total of 518 MRI examinations from 518 women (median age, 53 years; IQR, 51–59 years) were analyzed. Of these, 435 women did not have breast cancer (125 false-positive findings [24%; 125 of 518] and 310 true-negative findings [60%; 310 of 518]). Of the 83 breast cancers, 79 were true-positive findings and four were false-negative findings (16%; 83 of 518). The 83 breast cancers included 68 invasive cancers (82%) and 15 ductal carcinomas in situ (18%). Table 1 shows the demographics and tumor characteristics of the studied population.

Pooled Sensitivity and Specificity per Protocol

Figure 3 shows the pooled sensitivity and specificity per incremental step of MRI. The sensitivity of the shortest abbreviated MRI protocol (step 1) showed no evidence of a difference from that of the full-protocol MRI (step 4) (step 1 vs step 4: 84.3% [95% CI: 77.7, 89.2] vs 85.9% [95% CI: 80.0, 90.3], respectively; $P = .68$). The sensitivities of the second (83.9%; 95% CI: 77.8, 88.6) and third (83.9%; 95% CI: 77.8, 88.6) incremental steps of MRI showed no evidence of a difference from full protocol (step 4) ($P = .60$ and .60, respectively). Similarly, the specificity of the shortest abbreviated protocol (step 1) showed no evidence of a difference from the full protocol (step 4) (step 1 vs step 4: 73.9% [95% CI: 70.7, 76.9] vs 75.8% [95% CI: 72.8, 78.5], respectively; $P = .39$). The specificities of the second (74.9%; 95% CI: 71.8, 77.8) and third (76.7%; 95% CI: 73.6, 79.4) incremental steps of MRI showed no evidence of a difference from full protocol (step 4) ($P = .69$ and .68, respectively). Figures 4 and 5 show representative abbreviated MRI (step 1) examples of true- and false-positive findings, respectively.

The sensitivity of the shortest abbreviated MRI protocol showed no evidence of a difference from full protocol across all readers (Table S1). Among the seven readers, the specificity of the shortest abbreviated MRI protocol of four readers showed no evidence of a difference from full protocol. One reader achieved a higher specificity (66.5%; 95% CI: 61.9, 70.8) while interpreting the shortest abbreviated MRI protocol compared

with the full protocol (59.7%; 95% CI: 55.0, 64.2) (P = .04), whereas two other readers achieved a lower specificity (72.5% [95% CI: 68.1, 76.2] and 75.8% [95% CI: 71.5, 79.6]) while interpreting the shortest abbreviated MRI protocol compared with full protocol (81.5% [95% CI: 77.6, 84.9] and 83.4% [95% CI: 79.6, 86.6]) (P = .002, P = .05).

Pooled Sensitivity and Specificity per Protocol for Invasive Cancers

Table 2 shows the pooled sensitivity and specificity per incremental step of MRI for the invasive breast cancers only. The sensitivity (87.3%; 95% CI: 80.7, 91.8) and specificity (72.8%; 95% CI: 69.6, 75.9) of the shortest abbreviated MRI protocol (step 1) showed no evidence of a difference from full protocol (step 4) (sensitivity and specificity, 88.3% [95% CI: 82.3, 92.4] [P = .78 compared with sensitivity of the shortest protocol] and 74.5% [95% CI: 71.5, 77.3] [P = .44 compared with specificity of the shortest protocol], respectively).

Pooled Sensitivity and Specificity for All Invasive and Ductal Carcinoma in Situ Breast Cancers

Table S2 shows the results of the sensitivity analysis; it shows pooled sensitivity and specificity, including all breast cancers (invasive and ductal carcinoma in situ), in which BI-RADS scores of 1, 2, or 3 were classified as results that were negative for cancer (ie, no recall), and BI-RADS scores of 4 or 5 were classified as results that were positive for cancer (ie, requiring recall for diagnostic workup). The pooled sensitivity (80.4%; 95% CI: 73.4, 86.0) of the shortest abbreviated MRI protocol (step 1) showed no evidence of a difference from full protocol (85.2%; 95% CI: 79.1, 89.7) (P = .25); the specificity also showed no evidence of a difference (shortest protocol vs full protocol, 79.3% [95% CI: 76.4, 81.9] vs 79.3% [95% CI: 76.4, 82.0], respectively; P = .97).

Reading Times

A total of 2072 examinations (518 examinations multiplied by four incremental steps) were performed. Figure 6 shows the pooled reading time per incremental step of MRI. The reading time of the shortest abbreviated MRI protocol (step 1) was shorter than the full protocol (step 4) (49.7 seconds [95% CI: 48.5, 50.9] vs 96.4 seconds [95% CI: 94.3, 98.5], respectively; P < .001). Therefore, the pooled reading time of the shortest abbreviated MRI protocol (step 1) was 48% shorter than full protocol (step 4). The reading time of the shortest abbreviated MRI protocol was shorter than the full protocol across all readers (Table S3).

Scanning Times

The combined scan completion times for the sequences included in step 1 (abbreviated) through step 4 (full protocol) were approximately 3.5, 8.5, 12.5, and 18.5 minutes, depending on the hospital and scanner vendor.

Interobserver Agreement

Table 3 shows interobserver agreement. In 52.6%–55.4% of the 518 examinations for each of the incremental steps, all seven radiologists agreed on the referral (whether to recall [BI-RADS score of 3, 4, or 5] or not to recall [BI-RADS score of 1 or 2]). The Fleiss

Table 1: Demographics and Tumor Characteristics of the Women Included from the Dense Tissue and Early Breast Neoplasm Screening (DENSE) Trial

Characteristic	Value
Demographics of total dataset	518
Median age (y)*	53 (51–59) [49–74]
Median BMI*	22 (20.5–23.8)
Socioeconomic status†	
Lowest	69 (14)
Low midrange	128 (26)
Midhigh range	120 (24)
Highest	179 (36)
Missing	22
Tumor characteristics of women with diagnosed breast cancer	83
Histologic type	
DCIS	15 (18)
Invasive ductal carcinoma	37 (45)
Invasive lobular carcinoma	11 (13)
Mixed invasive ductal and lobular carcinoma	8 (10)
Tubular carcinoma	7 (8)
Other invasive carcinoma	5 (6)
Axillary lymph node status	
Negative	72 (87)
Positive	11 (13)
Tumor stage	
Early (0 or 1)	74 (89)
Late (2, 3, or 4)	9 (11)
Tumor grade	
DCIS	
1, Well-differentiated	6 (8)
2, Moderately differentiated	6 (8)
3, Poorly differentiated	3 (4)
Missing data or could not be assessed	0
Invasive	
1, well-differentiated	31 (40)
2, moderately differentiated	26 (34)
3, poorly differentiated	5 (6)
Missing data or could not be assessed	6
Receptor status (invasive breast cancer, n = 68)	
Positive for estrogen receptor, progesterone receptor, or both	59 (89)
ERBB2 (formerly HER2) enriched	3 (5)
Triple negative	4 (6)
Missing data	2

Note.—Unless otherwise indicated, data are numerators and data in parentheses are percentages. BMI = body mass index (calculated as weight in kilograms divided by height in meters squared), DCIS = ductal carcinoma in situ.

* Data in parentheses are IQRs; data in brackets are ranges.

† Socioeconomic status was determined according to quartile based on the distribution of the Dutch population in 2014. Data were available for postal codes in neighborhoods with more than 100 households. Quartile 1, lowest; quartile 2, low midrange; quartile 3, midhigh range; quartile 4, highest.

κ was between 0.56 and 0.59 across all incremental steps of MRI, corresponding to a moderate agreement. The highly overlapping 95% CIs suggest that there is no difference in interobserver agreement among the four incremental steps of MRI. Table S4 shows the agreement between the two readers who showed the highest level of concordance. The agreement between readers 2 and 3 across all incremental steps of MRI was approximately 86%. The Fleiss κ was between 0.63 and 0.66 across the four incremental steps of MRI, which reflects a substantial agreement. In Table S4, the highly overlapping 95% CIs of the Fleiss κ suggest that there is no difference in interobserver agreement among the four incremental steps of MRI.

Discussion

Costs and time implementing breast MRI in breast cancer screening programs may be reduced by using an abbreviated MRI protocol. The full multiparametric MRI protocol of the Dense Tissue and Early Breast Neoplasm Screening trial provides an opportunity to study the accuracy of various abbreviated MRI protocols in a reader study. In a secondary analysis of 518 screening breast MRI examinations from the DENSE trial in female participants with extremely dense breasts and results negative for

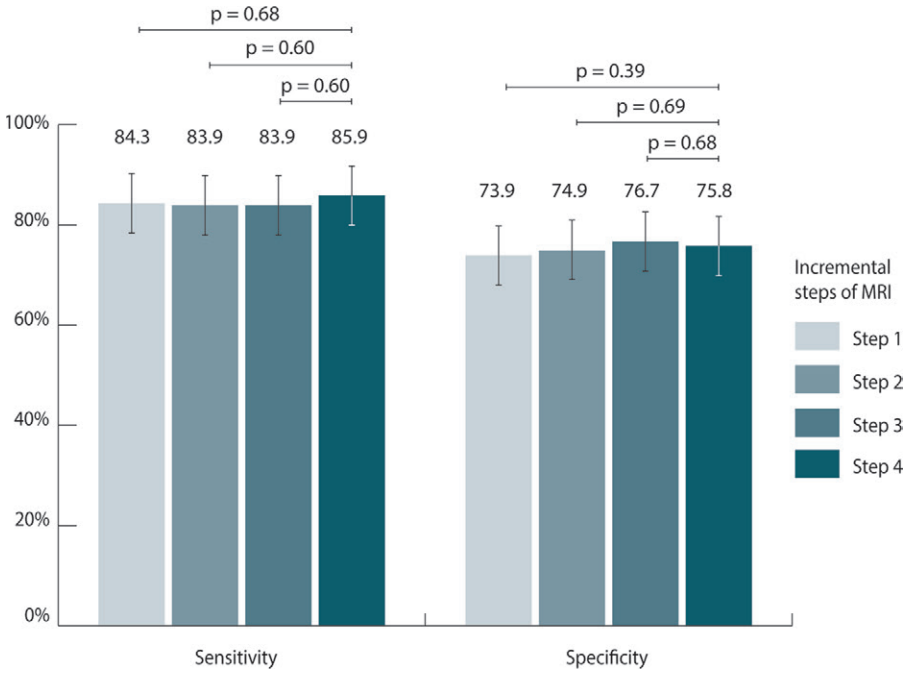

Figure 3: Bar graphs show pooled sensitivity and specificity per incremental steps of MRI. There was no evidence of a difference in both sensitivity and specificity between the abbreviated protocols and full MRI protocol.

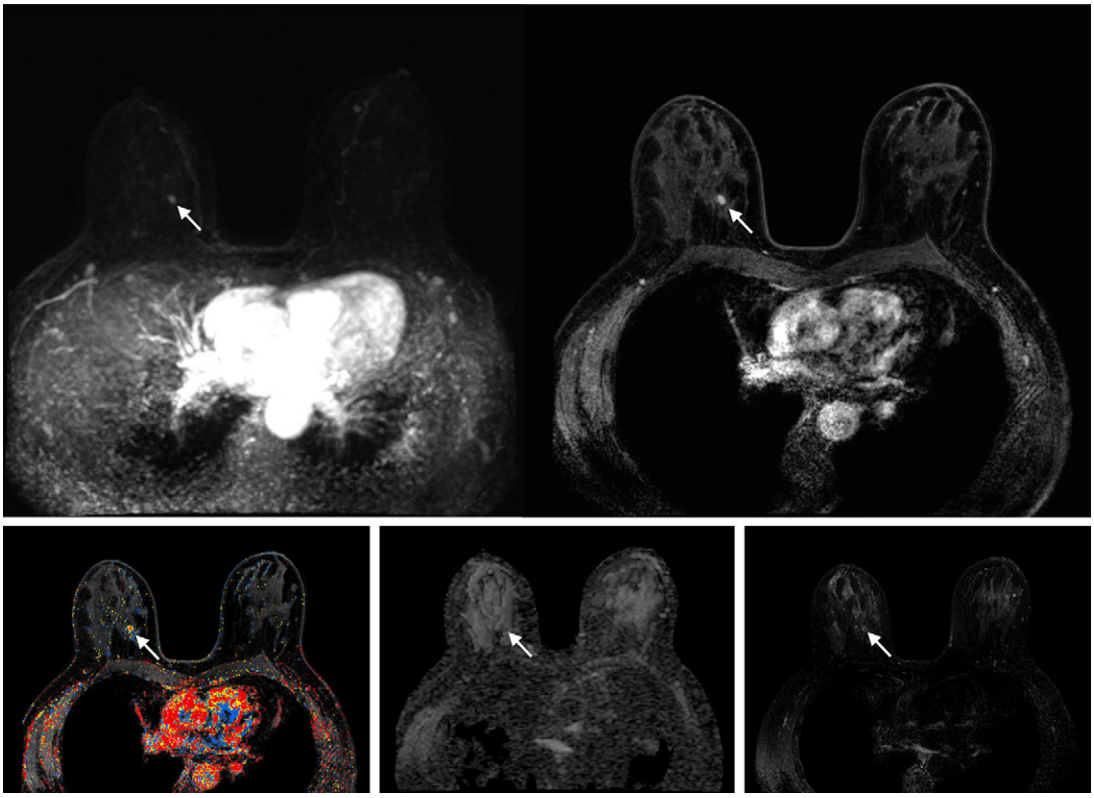

Figure 4: Abbreviated axial MRI images show a 6-mm irregular mass with an irregular margin (arrows) in the right upper inner quadrant with early rapid enhancement. The lesion was assessed as Breast Imaging Reporting and Data System (or BI-RADS) category 4 (suspicious for cancer). The participant was recalled and underwent US-guided core-needle biopsy that showed invasive carcinoma of no special type. On the full-protocol sequences (not shown), the lesion was T2-weighted hypointense and showed diffusion restriction and washout kinetics in the delayed phase, characteristics that, although are all confirmative of the malignant nature of the lesion, offered no additional value for making the recall decision.

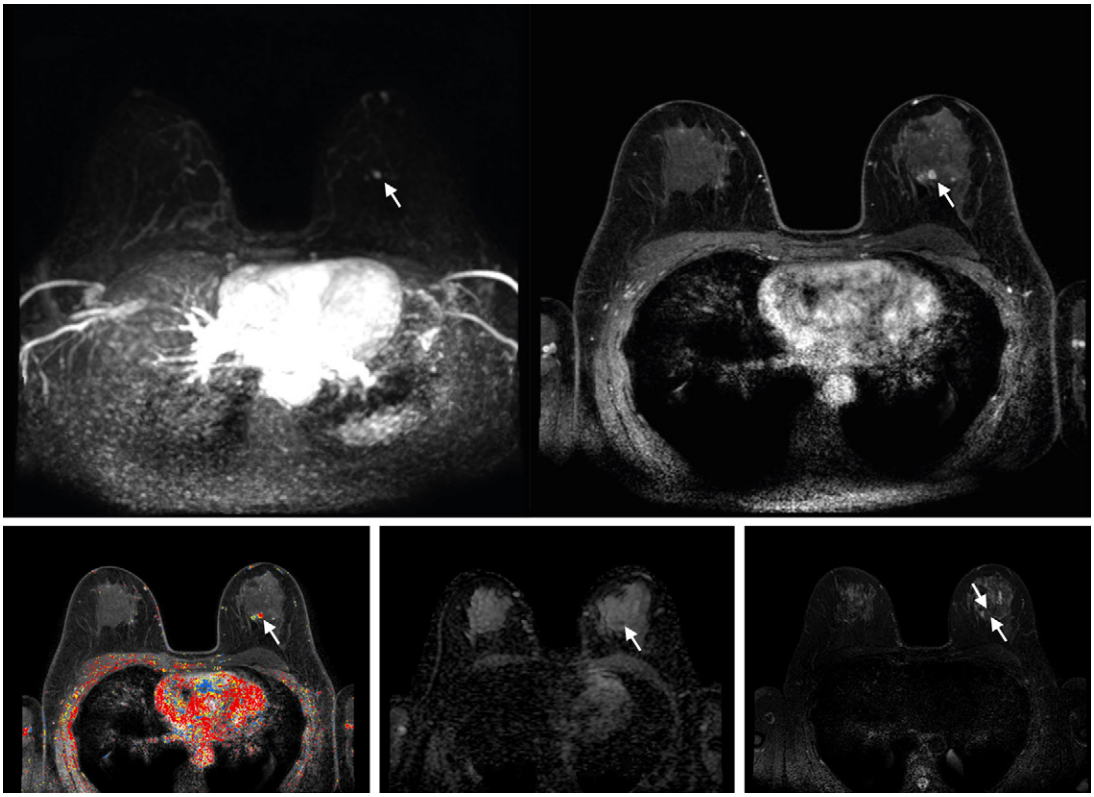

Figure 5: Abbreviated axial MRI images show a 7-mm irregular mass with irregular margin (arrows) in the right upper inner quadrant with early rapid enhancement (Breast Imaging Reporting and Data System category 4 [suspicious for cancer]). The participant was recalled and underwent an MRI-guided vacuum-assisted biopsy that showed sclerosing adenosis with microcalcifications and usual ductal hyperplasia and focal apocrine metaplasia. On the full-protocol images (not shown), the lesion was T2-weighted hypointense and showed diffusion restriction and washout kinetics in the delayed phase, characteristics that would not have reversed the decision to recall the participant.

Table 2: Pooled Sensitivity and Specificity of the Invasive Breast Cancers Only Compared with the Pooled Sensitivity and Specificity of All Breast Cancers

Incremental Step of MRI	Sensitivity (%)	Specificity (%)
Invasive breast cancers only (*n* = 68)		
1	87.3 (80.7, 91.8) [.78]	72.8 (69.6, 75.9) [.44]
2	86.5 (80.2, 90.9) [.62]	73.8 (70.6, 76.7) [.74]
3	86.7 (80.5, 91.9) [.66]	75.5 (72.4, 78.3) [.65]
4	88.3 (82.3, 92.4)	74.5 (71.5, 77.3)
All breast cancers: invasive (*n* = 68) and DCIS (*n* = 15)		
1	84.3 (77.7, 89.2) [.68]	73.9 (70.7, 76.9) [.39]
2	83.9 (77.8, 88.6) [.60]	74.9 (71.8, 77.8) [.69]
3	83.9 (77.8, 88.6) [.60]	76.7 (73.6, 79.4) [.68]
4	85.9 (80.0, 90.3)	75.8 (72.8, 78.5)

Note.—Data in parentheses are 95% CIs and data in brackets are *P* values. *P* values were calculated with a generalized estimating equation model. Step 1: The first step consisted of the dual high-temporal low-spatial and low-temporal high-spatial dynamic T1 series, from before contrast injection to 120 seconds after contrast injection only. Step 2: The second step added diffusion-weighted images to the series available from step 1. Step 3: The third step added T2-weighted images to the series available from steps 1 and 2. Step 4: The fourth and final step added non–fat-saturated T1-weighted precontrast images, all remaining dynamic phases acquired after the first 120 seconds after contrast administration, and enhancement curve kinetics to the series available from steps 1, 2, and 3. This final step is the full multiparametric breast MRI protocol that was used in the Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial. DCIS = ductal carcinoma in situ.

cancer at mammography, seven radiologists performed incremental readings. This included abbreviated (dynamic T1-weighted series up to 120 seconds after contrast agent injection) and full multiparametric protocols. Abbreviated and full MRI protocols had comparable sensitivity (84.3% vs 85.9%, respectively; *P* = .68) and specificity (73.9% vs 75.8%, respectively; *P* = .39). Abbreviated MRI had almost 50% shorter pooled reading time (49.7 seconds vs 96.4 seconds, respectively; *P* < .01) and 70%–80% shorter scanning time, depending on hospital and scanner vendor. Our results suggest that in a screening setting, the additional sequences, including diffusion-weighted imaging, T2-weighted imaging, and delayed contrast-enhanced T1-weighted images with curve kinetics, do not provide additional diagnostic information for making a recall or no-recall decision.

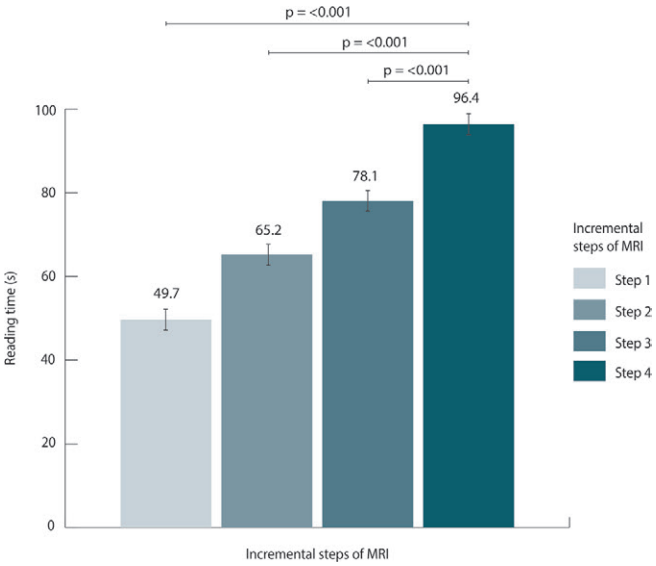

Figure 6: Bar graph shows pooled reading time (in seconds) per incremental step of MRI. The abbreviated protocol had an almost 50% shorter pooled reading time than the full protocol.

Table 3: Interobserver Agreement Presented as the Percentage of Agreement and Fleiss κ

Incremental Step of MRI	Percentage of Agreement (%)	Fleiss κ*
1	55.4	0.59 (0.54, 0.63)
2	53.6	0.57 (0.53, 0.61)
3	54.8	0.57 (0.53, 0.62)
4	52.6	0.56 (0.51, 0.60)

Note.—Data in parentheses are 95% CIs. Step 1: The first step consisted of the dual high-temporal low-spatial and low-temporal high-spatial dynamic T1 series, from before contrast injection to 120 seconds after contrast injection only; step 2: The second step added diffusion-weighted images to the series available from step 1; Step 3: The third step added T2-weighted images to the series available from steps 1 and 2; and step 4: The fourth and final step added non–fat-saturated T1-weighted precontrast images, all remaining dynamic phases acquired after the first 120 seconds after contrast administration, and enhancement curve kinetics to the series available from steps 1, 2, and 3. This final step is the full multiparametric breast MRI protocol that was used in the Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial.

* Interpretation of Fleiss κ: 0–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.81–1.00 almost perfect agreement.

Whereas our results contrast with previous studies (23,24) that showed mainly improved specificity by adding T2 and diffusion-weighted imaging, it should be noted that these studies mainly reported patients with known (ie, large) lesions and did not specifically focus on the screening setting with mainly subcentimeter lesions. In our study, we show that the most abbreviated MRI protocol (step 1) maintained diagnostic accuracy while reducing reading and scanning times in MRI from a population-screening setting.

The sensitivities and specificities (across all incremental steps of MRI) in this reader study were lower than the true sensitivity and specificity observed in the prospective real-life screening setting of the DENSE trial. This difference cannot be explained by a difference in reader experience because all radiologists in this reader study also participated in the DENSE trial. Instead, it is an expected and likely result of the challenging case set and the high workload: the case set not only contained all breast cancers from the DENSE trial but also many false-positive findings. Additionally, radiologists were required to read this comparatively high proportion of complex cases in a high-throughput setting of around 250 cases per day. The observation that performance in a reader study is lower than in a real-life screening setting is unsurprising and consistent with previous research (25) comparing the performance of readers in reader studies with their performance in clinical practice. These studies have consistently shown that performance of radiologists in reader studies is poorer than in screening practice (25). Conversely, Comstock et al (15), who studied abbreviated MRI protocols in a prospective real-life screening setting that also involved asymptomatic women with dense breasts, reported a sensitivity of 95.7% and a specificity of 86.7%. This aligns with the finding that the diagnostic accuracy in a real-life screening setting is higher than that observed in a reader study.

We anticipate that the large fraction of cases with false-positive findings, in combination with the already challenging setting of interpreting 518 consecutive examinations in 2072 individual steps, also contributed to the overall moderate level of interobserver agreement observed across all four incremental steps. Furthermore, it is important to note that in a screening scenario, MRI scans are not assessed by seven radiologists. Thus, similar to the diagnostic accuracy, interobserver agreement cannot be directly compared with the real-life screening situation. A more important finding is that an abbreviated MRI protocol appears to have no effect on the interobserver agreement.

A systematic review conducted by Hernández et al (18) summarized the findings from multiple abbreviated MRI studies. Overall, despite variations in protocols, study populations, and objectives, the diagnostic accuracy of abbreviated MRI protocols was found to be comparable with that of full-protocol MRI (18). The studies included in the review tended to use noncontrast T1-weighted or T2-weighted sequences and at least one contrast-enhanced sequence. Other more recent reader studies (16,19,20) showed similar results compared with the results of the systematic review and of our reader study. Thus, the general finding (ie, that an abbreviated MRI protocol has a diagnostic accuracy comparable with that of a full protocol) is consistent with our findings.

The highly abbreviated MRI protocol reduced scanning time to approximately 20% of that required for the multiparametric MRI protocol, allowing more participants to be scanned within a shorter time frame, thereby potentially addressing capacity issues associated with full MRI protocols. However, it is important to note that implementing this protocol requires efforts to optimize workflow for efficient screening and manage capacity effectively. Besides these practical considerations, implementing abbreviated MRI protocols is expected to positively impact women's experiences. Both the time spent in the MRI unit and high noise levels have been identified as sources of discomfort and reasons for discontinuing full-protocol MRI screening (26,27). Therefore, reducing the examination time and noise levels could potentially improve the patient experience and may contribute to higher attendance rates. Whereas many studies have focused on a single

variant of abbreviated MRI protocol, our study emphasizes the optimization of the MRI protocol.

Our study had limitations. First, although we used prospectively acquired population screening data from the DENSE trial, the complexity of the case mix and the challenging nature of the retrospective reading setting make the results not directly comparable with a prospective real-world screening setting. Second, the stepwise setup may not completely accurately reflect the diagnostic accuracy of reading a full multiparametric MRI at once, without having to provide BI-RADS scores for prior incremental reading steps.

In conclusion, this multireader study in women from the Dense Tissue and Early Breast Neoplasm Screening trial with extremely dense breasts and results at mammography that were negative for cancer showed that diagnostic accuracy of a highly abbreviated breast MRI protocol for first-round screening was comparable to that of a full multiparametric MRI protocol, at much shorter reading and scanning times. These shorter reading and scanning times may allow for implementation of abbreviated MRI protocols in national screening programs. A prospective multicenter trial to confirm these results and validate the performance of the shortest abbreviated MRI protocol in real-life population screening started inclusion of participants in 2024.

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