Study Protocol

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Diffusion-Weighted Magnetic Resonance Imaging for Breast Cancer Screening in High-Risk Women: Design and Imaging Protocol of a Prospective Multicenter Study in Korea

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ABSTRACT

Purpose: Interest in unenhanced magnetic resonance imaging (MRI) screening for breast cancer is growing due to concerns about gadolinium deposition in the brain and the high cost of contrast-enhanced MRI. The purpose of this report is to describe the protocol of the Diffusion-Weighted Magnetic Resonance Imaging Screening Trial (DWIST), which is a prospective, multicenter, intraindividual comparative cohort study designed to compare the performance of mammography, ultrasonography, dynamic contrast-enhanced (DCE) MRI, and diffusion-weighted (DW) MRI screening in women at high risk of developing breast cancer.
Methods: A total of 890 women with *BRCA* mutation or family history of breast cancer and lifetime risk ≥ 20% are enrolled. The participants undergo 2 annual breast screenings with digital mammography, ultrasonography, DCE MRI, and DW MRI at 3.0 T. Images are independently interpreted by trained radiologists. The reference standard is a combination of pathology and 12-month follow-up. Each image modality and their combination will be compared in terms of sensitivity, specificity, accuracy, positive predictive value, rate of invasive cancer detection, abnormal interpretation rate, and characteristics of detected cancers. The first participant was enrolled in April 2019. At the time of manuscript submission, 5 academic medical centers in South Korea are actively enrolling eligible women and a total of 235 women have undergone the first round of screening. Completion of enrollment is expected in 2022 and the results of the study are expected to be published in 2026.
Discussion: DWIST is the first prospective multicenter study to compare the performance of DW MRI and conventional imaging modalities for breast cancer screening in high-risk women. DWIST is currently in the patient enrollment phase.

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Conflict of Interest
The authors declare that they have no competing interests.

Author Contributions
Conceptualization: Shin HJ, Moon WK; Data curation: Shin HJ, Lee SH, Park SY, Moon WK; Formal analysis: Shin HJ, Lee SH, Moon WK; Funding acquisition: Shin HJ, Moon WK; Investigation: Shin HJ, Lee SH, Park VY, Yoon JH, Kang BJ, Yun BL, Kim TH, Ko ES, Han BK, Chu AJ, Park SY, Kim HH, Moon WK; Methodology: Shin HJ, Park SY, Moon WK; Project administration: Shin HJ, Moon WK; Resources: Shin HJ, Moon WK; Software: Shin HJ; Writing - original draft: Shin HJ, Moon WK; Writing - review & editing: Shin HJ, Lee SH, Park VY, Yoon JH, Kang BJ, Yun BL, Kim TH, Ko ES, Han BK, Chu AJ, Park SY, Kim HH, Moon WK.

INTRODUCTION

Mammographic screening detects breast cancer at an early stage and thus leads to reductions in breast cancer-related mortality [1]. However, women at higher risk of breast cancer such as young women with dense breast tissue in whom mammography is less sensitive can benefit from undergoing other screening modalities [2]. Dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) is a highly sensitive modality for breast cancer detection and is recommended as a supplemental screening tool for women with *BRCA* mutations or a family history of breast cancer and a lifetime risk of over 20% [2]. A systematic review showed that the combined use of DCE MRI and mammography improved the sensitivity of breast cancer detection by mammography from 39% to 94%, while the specificity decreased from 95% to 77% [3]. Despite the notable benefits of DCE MRI, only a small fraction of high-risk women are undergoing breast MRI [4]. The widespread use of MRI is limited by its high cost and long acquisition time, which are mostly related to the use of contrast agents [5]. Furthermore, although no conclusion has been reached regarding the safety of repeated gadolinium exposure from DCE MRI, the recent discovery of the deposition of gadolinium-based contrast agents in the brain and other body tissues raised public concerns regarding the safety of DCE MRI as a life-long screening modality for healthy and relatively young populations [6].

Ultrasonography can be considered for those who qualify for but cannot undergo MRI [2]. However, it is relatively operator-dependent and has a low cancer detection rate, high abnormal interpretation rate (AIR), and low positive predictive value (PPV) for biopsy recommendation [7]. Therefore, the development of a fast, inexpensive, and safe unenhanced screening tool such as diffusion-weighted (DW) MRI for complementing mammography has become clinically important to make breast MRI more broadly available for breast cancer screening in high-risk women.

DW MRI is a fast, functional modality that measures the movement of water molecules to create tissue contrast without the need for an external contrast agent injection [8]. Diffusion restriction occurs in tissues with high cellular densities such as malignancy, and is depicted as a hyperintense area on DW MRI [9]. Previous studies showed that the apparent diffusion coefficient (ADC) values calculated from DW MRI enabled accurate differentiation between benign and malignant lesions [10]. As such, multiple studies explored the use of DW MRI as a stand-alone tool by using study designs that simulate the clinical screening setting [11-18] and demonstrated its usefulness in detecting small breast cancer in women with intermediate-to-high risks [15-18]. In previous blinded reader studies, however, DW MRI showed varying degrees of sensitivity (45%–94%) and specificity (79%–95%) [5,11,18]. The main reason for the low sensitivity of DW MRI compared with DCE MRI is its low detection rate for invasive cancers that are less than 1 cm in size and ductal carcinoma *in situ* (DCIS), of which DCIS may be related to overdiagnosis in breast cancer screening [5,13,19]. Recent studies with 3.0 T DW MRI scanners and multi-shot echo-planar imaging sequences reported a significantly higher sensitivity to subcentimeter invasive cancers compared with previous studies that used 1.5 T DW MRI scanners [5,11,16,18]. However, these studies were retrospective in nature

and the results were based on small 5single-center studies. A prospective multicenter trial with standardized acquisition and interpretation protocols in a large population is needed to determine the efficacy of high-resolution DW MRI for breast cancer screening.

In the Diffusion-Weighted Magnetic Resonance Imaging Screening Trial (DWIST), we hypothesized that the sensitivity of the current high-resolution DW MRI in 3.0 T scanners is likely higher than that of mammography or ultrasonography, but lower than that of DCE MRI [15,16,18,20]. However, low-cost and safer DW MRI could be used as an alternative to DCE MRI for breast cancer screening in high-risk women, provided that there are no significant differences between DCE MRI and DW MRI in the detection rate of invasive cancer. The purpose of this report is to describe the protocol of the DWIST, which is a multicenter study designed to compare, among the same participants, the performance of mammography, ultrasonography, DCE MRI, and DW MRI screening in women at high risks of developing breast cancer.

METHODS

The study is financially supported by a grant from the National R&D Program for Cancer Control, Ministry of Health and Welfare, Republic of Korea (HA17C0056). This study protocol received approval from the Institutional Review Boards (IRBs; D-1809-134-976) of the participating centers and obtain written consent for publication of these data (mammography, ultrasonography, MR images, clinical data including age, BRCA mutation, family history of breast cancer) from all participants.

Study design
The DWIST is a prospective multicenter, intraindividual comparative cohort study. Participants will be recruited from 8 academic medical centers in South Korea—Seoul National University Hospital, Asan Medical Center, Severance Hospital, Catholic University of Korea Seoul, Samsung Medical Center, Boramae Medical Center, Seoul National Bundang Hospital, and Ajou University Hospital. The participating institutions are required to have the latest 3.0 T MRI scanners and comply with the Korean quality assurance guidelines for medical images. Radiologists will be required to successfully complete a training case series of 100 DW MR studies prior to interpreting the DW MRI results. The flow chart of the study design and the schedule of imaging is presented in **Figure 1**. Each eligible participant undergoes 2 annual breast screenings with digital mammography, ultrasonography, DCE MRI, and DW MRI, and the acquired images are read independently. Pathology of core or surgical biopsy and 1-year follow-up are used as the reference standard for PPV, rate of invasive cancer detection, and AIR. Interval cancers are included in the reference standard for sensitivity and specificity [21]. Data are collected using the electronic case report form (eCRF) (**Supplementary Data 1**).

Ethical consideration
The study protocol was approved by IRB of 8 participating institutions. This protocol was first approved by the IRB of Seoul National University Hospital in November 2018, and registered in an international trial registry (ClinicalTrials.gov number: NCT03835897) in February 11th 2019. Written informed consent was obtained from all participants by investigators. The first participant was enrolled in April 2019. At the time of manuscript submission (February, 2021), active inclusion of patients is ongoing in 5 centers (Seoul National University Hospital,
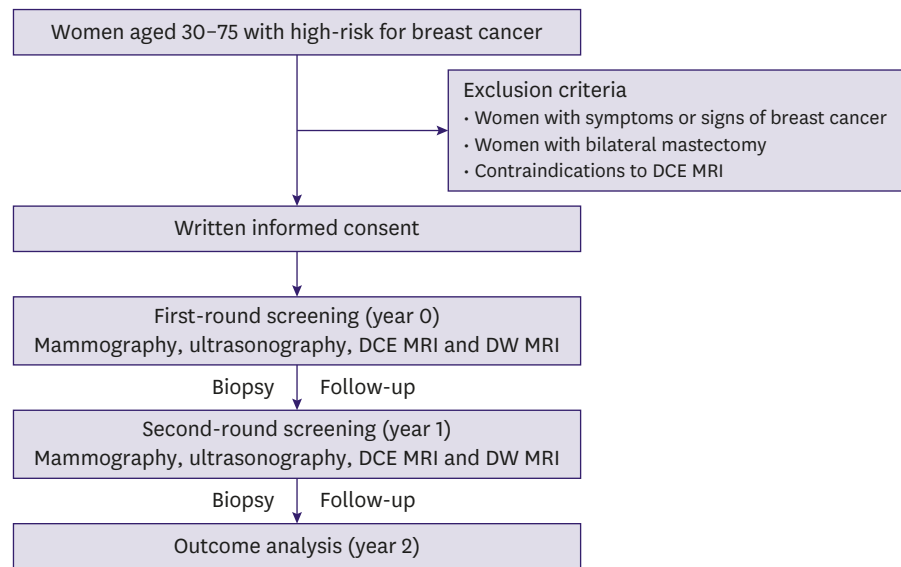
Figure 1. Study flow chart.
DCE = dynamic contrast-enhanced; MRI = magnetic resonance imaging; DW = diffusion-weighted.

Asan Medical Center, Severance Hospital, Catholic University of Korea Seoul, and Seoul National University Bundang Hospital) and a total of 235 women have been enrolled and have undergone the first round of screening. Enrollment completion is expected in 2022, and the study results are expected to be presented in 2026.

Study population

Asymptomatic women aged 30 to 75 years at high risk for breast cancer are eligible for inclusion in this study. Specifically, women meeting any one of the following criteria are included in the study; *BRCA* mutation carrier or untested first-degree relative of *BRCA* mutation carrier; family history of breast cancer in first- or second-degree relatives and a lifetime risk ≥ 20% calculated by the Tyrer-Cuzick model [22]; history of breast cancer and family history of breast cancer in first- or second-degree relatives; history of lobular carcinoma in situ, atypical ductal hyperplasia, or atypical lobular hyperplasia on previous biopsy or surgery and a lifetime risk ≥ 20% calculated by the Tyrer-Cuzick model; and those who received thoracic radiation therapy between the ages of 10 and 30.

The exclusion criteria are as follows: symptoms or signs of breast cancer or recurrence; bilateral mastectomy; pregnant or breast-feeding; underwent chemotherapy due to malignancy in other organs; and contraindications to MRI including claustrophobia, renal insufficiency (estimated glomerular filtration rate < 30 mL/min/1.73m^2), metallic foreign bodies (e.g., pacemaker or clips), history of severe side effects due to MRI contrast agent, and who cannot tolerate 40 minutes scanning time.

Imaging acquisition

Mammography in two standard image planes is performed with digital mammography units. Attending breast radiologists perform the ultrasonography using 5–18 MHz hand-held transducers or automated whole-breast scanners. Breast MRI is performed in the prone position on 3.0 T MRI scanners with a dedicated 16- or 18-channel breast coil (**Table 1**, **Supplementary Data 2**).

Table 1. DCE and DW MRI protocols of the DWIST

Parameter	DCE MRI	DW MRI
Equipment		
Magnet field strength	3.0 T	
Type of coil	Double-breast, 16- or 18-channels	
Acquisition parameter		
Orientation	Axial	Axial
In-plane resolution	$\leq 1 \times 1$ mm^2	$\leq 1.3 \times 1.3$ mm^2
Slice thickness	≤ 1 mm	≤ 3 mm
Imaging sequences	T2, preT1, T1 DCE, delayed T1	EPI with b values of 0, 800, 1,200 sec/mm^2
Post-processing		
Subtraction	Postcontrast series minus precontrast series	NA
ADC map	NA	0 and 800 sec/mm^2
MIP	Axial and sagittal	Axial and sagittal
Acquisition time	15–20 minutes	6–7 minutes

DCE = dynamic contrast-enhanced; DW = diffusion-weighted; MRI = magnetic resonance imaging; DWIST = Diffusion-Weighted Magnetic Resonance Imaging Screening Trial; EPI = echo-planar imaging; NA = not applicable; ADC = apparent diffusion coefficient; MIP = maximum intensity projection.

For DW MRI screening, 3 b values of 0, 800, and 1,200 sec/mm^2 are used [5,23] and both the single- and the multi-shot echo-planar imaging sequence are optimized with an in-plane resolution of 1.3×1.3 mm, slice thickness of 2.5–3 mm with no gap, and enough slices to cover both breasts in the axial dimension (**Table 1**). The acquisition time is 6–7 minutes, and ADC maps are generated based on the b values of 0 and 800 sec/mm^2 DW MRI data. The resulting DW MRI images are reconstructed into single summation images with maximum-intensity projections (MIPs) in the sagittal and axial planes. A table summarizing the DW MRI sequences from the three MRI vendors used in the DWIST is provided in **Supplementary Data 2**.

Image interpretation

Breast radiologists at each site who are blinded to the results of the other studies independently interpret the mammography, ultrasonography, DCE MRI, and DW MRI according to the Breast Imaging Reporting and Data System (BI-RADS) lexicon and final assessment category [21] and also record the likelihood of malignancy (score range, 0%–100%; higher scores indicate higher possibilities of malignancy). Radiologists interpreting the DW MRI are provided with the DWIST DW MRI interpretation guidelines in order to standardize the interpretation across institutions. The DW MRI interpretation guidelines have been constructed based on qualitative and quantitative assessments (**Figure 2**) that include three criteria (i.e., morphology, internal characteristics, and diffusion level) [24]. Then, a site investigator records a combined category after reviewing 1) mammography and ultrasonography, 2) mammography and DCE MRI, 3) mammography and DW MRI, and 4) DCE MRI and DW MRI. The combined category is determined as the more suspicious category between the two modalities. For DW MRI, it is also determined whether adding precontrast T2-weighted imaging or T1-weighted-imaging results in a significant change in the assessment. The details of image interpretation and management of lesions are presented in **Supplementary Data 2**.

Main outcome and measures

The primary outcome is the sensitivity of mammography, ultrasonography, DCE MRI, and DW MRI for the detection of breast cancer. Secondary outcomes are the rate of invasive cancer detection, specificity, PPV, and AIR of mammography, ultrasonography, DCE MRI, and DW MRI, interval cancer rate, and the characteristics of detected cancers. The outcome measures of mammography and the combinations of other imaging modalities will also be
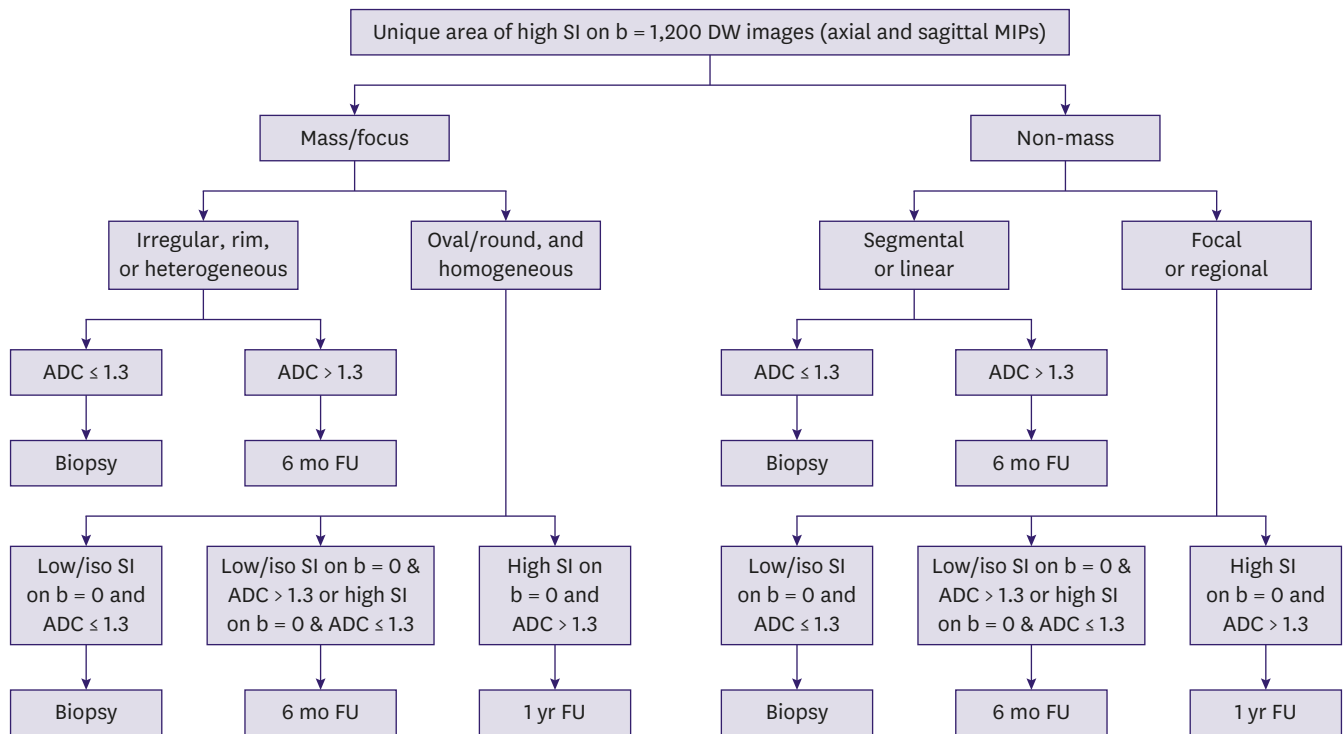
Figure 2. DW MRI interpretation guideline.
Note: ADC map is calculated from b = 0 and 800 sec/mm² DW image, and the unit for the ADC value is (× 10⁻³ mm²/sec). An ADC cutoff of 1.3 was determined based on a diffusion level lexicon from EUSOBI guidelines [29] in order to decrease false positive and increase cancer detection.
DW = diffusion-weighted; MRI = magnetic resonance imaging; ADC = apparent diffusion coefficient; MIP = maximum-intensity projection; FU = follow-up; SI = signal intensity.
*These algorithms are not meant to dictate individual case management decisions. The ultimate decision regarding DW-MR interpretation must be made by the interpreting radiologist, taking into consideration all of the circumstances presented in an individual examination. Reprinted, with permission from [30].

compared. In addition, the outcome measures of DCE MRI will be compared with those of DCE MRI and DW MRI combination. In addition, the main outcome measures in the first (prevalence) and second (incidence) screening rounds will be compared. Further information on the definition of the outcome measures are shown in **Supplementary Data 2**.

Sample size/power calculation

The sample size of the study was chosen using the McNemar's test to provide 80% power to detect a difference in the sensitivity between mammography and DW MRI with a significance level of 0.05. As there are no published studies on the sensitivity of DW MRI in the screening population among women at high risk, we estimated that the sensitivity of screening DW MRI for breast cancer detection would be 72.5%, which is approximately 80% of the sensitivity of DCE MRI (90%), based on previous studies [18,25]. For mammography, we assumed sensitivity of 37.5%. The required number of breast cancers to detect a difference in sensitivity between mammography and DW MRI is 49 when considering an attrition rate of 10%; assuming the cancer prevalence among high-risk women as 2.9%, 1,690 examinations are needed to obtain 49 cancers. Assuming that about 10% of the participants would drop out and not receive a second screening, a total of 890 participants will provide 890 + 801 = 1,691 examinations.

Screening failure and drop-out criteria

Patients who have withdrawn their informed consent prior to the first round of examinations will be regarded as a screening failure. If patients do not receive the next tests within one

month before or after the appropriate interval from the previous test data, they will be disqualified and labeled dropouts.

Data collection

Data will be collected using eCRF (http://dwi.crf.kr). Investigators or designated qualified staff in each institution will enter patient data obtained from mammography, breast ultrasonography, DCE MRI, and DW MRI during surveillance into eCRF. A valid username and password are needed to log into the eCRF system to secure patient data. Each patient is automatically assigned a unique identification number at the time of enrollment according to the institution and registration order.

Statistical methods

Continuous variables will be summarized with standard descriptive statistics including mean, standard deviation, median, and interquartile range. For categorical variables, counts and proportions will be reported. Because each patient will be examined by different imaging techniques, the sensitivity, specificity, rate of invasive cancer detection, and AIR will be compared using the McNemar's test for intraindividual comparison. PPVs will be reported and compared using 95% confidence intervals. All reported *p*-values will be two-sided. A post hoc Bonferroni adjustment will be used for multiple comparisons of the primary and secondary outcomes (a total of 4 comparisons), with *p*-values < 0.0125 considered statistically significant. Depending on the data distribution, continuous variables will be analyzed using the Student's *t*-test or Mann-Whitney *U* test for independent data, and categorical variables will be analyzed using the χ^2 test. The area under the receiver operating characteristic (ROC) curves (AUCs) were estimated and compared using the method accounting for the correlation. All statistical analysis will be performed in R software, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

DISCUSSION

We here present the design and imaging protocol of the DWIST. Although breast MRI is recommended in addition to mammography for women with high risks for breast cancer, MRI is currently underutilized due to high costs and the lack of availability. To enable wider use of breast MRI and improve its cost-effectiveness, MRI protocols that are less time-consuming and less costly should be developed [26]. Accordingly, the concept of abbreviated breast MRI was introduced and showed comparable results with DCE MRI [27]. However, abbreviated breast MRI still relies on the use of intravenous contrast agents; this is time-consuming, costly, painful, and carries a risk for complications including gadolinium deposition in the brain despite the fact that the macrocyclic contrast agents currently used are very stable compared with linear contrast agents [6]. The use of intravenous contrast agents is also contraindicated in pregnant women and patients with renal impairment or gadolinium allergy [6]. Therefore, there is an urgent need for the development of MRI techniques that do not rely on the administration of contrast agents such as DW MRI.

The DWIST is designed to compare the performance of mammography, ultrasonography, DCE MRI, and DW MRI for breast cancer screening in the same participants. We hypothesized that DW MRI as a stand-alone screening test is superior to mammography or ultrasonography for detecting clinically occult cancer. We also expect that the sensitivity of the current state-of-the-art DW MRI would be at least 80% of that of DCE MRI, and the rate

of invasive cancer detection and the specificity should be similar between the two modalities [18]. Considering that we will also compare the outcome measures of mammography/ultrasonography combinations, mammography/DCE MRI combinations, mammography/DW MRI combinations, and DCE/DW MRI combinations, the DWIST will determine whether ultrasonography can play a role in breast cancer screening in high-risk women. It will also be possible to see whether multiparametric MRI with DW MRI can reduce the high false positive rate of DCE MRI.

The DWIST strictly requires the participating institutions to be equipped with the latest 3.0 T MRI scanner, because high spatial resolution DW MRI images with less noise and artifacts are essential for detecting small cancers [27]. The high-resolution DW MRI sequence is optimized to have an in-plane resolution of 1.3 × 1.3 mm and a slice thickness of 2.5–3 mm. In addition, three b-values are selected to optimize both the specificity and sensitivity of DW MRI as a screening test. Specifically, the b-values of 0 and 800 sec/mm^2 are used for creating ADC maps for lesion characterization and the b-value of 1200 sec/mm^2 is used for lesion visualization [5,24]. In addition, the sagittal and axial MIPs obtained through the post-imaging process will enable rapid detection of suspicious lesions. In order to ensure the image quality of the participating institutions, which is important for multicenter MRI studies, the phantom and clinical patient images will be used to evaluate the consistency between the DW MRI image quality and ADC measurements of the participating institutions [28]. The DW MRI interpretation protocol is also standardized to minimize the rate of false-positive readings and biopsy recommendations for benign lesions without missing out on invasive cancer. Radiologists participating in the readings will be sufficiently trained and be required to pass the appropriate certification tests.

Overdiagnosis of indolent lesions has recently been recognized as a major detriment in cancer screening [29]. Overdiagnosis on mammography and MRI screening is usually driven by low- or intermediate-grade DCIS that are detected as microcalcifications or non-mass enhancement findings, respectively [30]. In contrast, DW MRI, a functional imaging technique that reflects the cellularity and tissue microstructure of breast cancers, has a similar sensitivity to DCE MRI in detecting mass or invasive cancer, but with significantly lower sensitivity for the detection of non-masses or DCIS [18,20]. In addition, high-grade DCIS tends to exhibit lower ADC and higher conspicuity on DW MRI than low- or intermediate-grade DCIS [5]. Therefore, using DW MRI as a screening tool may reduce the overdiagnosis of DCIS without missing biologically important invasive cancers [30].

The low sensitivity of DW MRI in small invasive breast cancers or some types of invasive lobular carcinomas has been a major obstacle to the widespread application of DW MRI as a screening tool [12,20]. However, the use of high-field strength scanners and the latest high-resolution DW MRI sequences can better detect and characterize breast lesions including subcentimeter cancers [5,11,16,18]. The DWIST researchers have been working to improve the spatial resolution of the DW MRI and are now able to obtain high-resolution images with a 0.7 × 0.7 × 2.5 mm reconstructed voxel size covering both breasts in less than 7 minutes using simultaneous multi-slice sequences (**Supplementary Data 2**). The DWIST will characterize the sensitivity profile of DW MRI by comparing the biological characteristics of the detected cancers between imaging modalities, including tumor histologic type, grade, and receptor status.

In summary, the DWIST is the first prospective multicenter cohort study to compare the performance of DW MRI and conventional imaging modality for breast cancer screening in

high-risk women. A standardized acquisition and interpretation protocol as well as a quality assurance program for DW MRI screening are in place. Patient enrollment is currently ongoing.

ACKNOWLEDGMENTS

SUPPLEMENTARY MATERIALS

Supplementary Data 1
Case report forms for study

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Supplementary Data 2
Supplementary methods

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REFERENCES

1. Oeffinger KC, Fontham ET, Etzioni R, Herzig A, Michaelson JS, Shih YC, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. JAMA 2015;314:1599-614.
   PUBMED | CROSSREF

2. Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast cancer screening in women at higher-than-average risk: recommendations from the ACR. J Am Coll Radiol 2018;15:408-14.
   PUBMED | CROSSREF

3. Warner E, Messersmith H, Causer P, Eisen A, Shumak R, Plewes D. Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. Ann Intern Med 2008;148:671-9.
   PUBMED | CROSSREF

4. Wernli KJ, DeMartini WB, Ichikawa L, Lehman CD, Onega T, Kerlikowske K, et al. Patterns of breast magnetic resonance imaging use in community practice. JAMA Intern Med 2014;174:125-32.
   PUBMED | CROSSREF

5. Amornsiripanitch N, Bickelhaupt S, Shin HJ, Dang M, Rahbar H, Pinker K, et al. Diffusion-weighted MRI for unenhanced breast cancer screening. Radiology 2019;293:504-20.
   PUBMED | CROSSREF

6. U.S. Food and Drug Administration (FDA). FDA drug safety communication: FDA warns that gadolinium-based contrast agents (GBCAs) are retained in the body; requires new class warnings. 2017. https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-gadolinium-based-contrast-agents-gbcas-are-retained-body. Accessed February 3rd, 2021.

7. Kim SH, Kim HH, Moon WK. Automated breast ultrasound screening for dense breasts. Korean J Radiol 2020;21:15-24.
   PUBMED | CROSSREF

8. Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. Radiology 1986;161:401-7.
   PUBMED | CROSSREF

9. Park MJ, Cha ES, Kang BJ, Ihn YK, Baik JH. The role of diffusion-weighted imaging and the apparent diffusion coefficient (ADC) values for breast tumors. Korean J Radiol 2007;8:390-6.
   PUBMED | CROSSREF

10. Baltzer PA, Bickel H, Spick C, Wengert G, Woitek R, Kapetas P, et al. Potential of noncontrast magnetic resonance imaging with diffusion-weighted imaging in characterization of breast lesions: intraindividual comparison with dynamic contrast-enhanced magnetic resonance imaging. Invest Radiol 2018;53:229-35.
PUBMED | CROSSREF

11. Yabuuchi H, Matsuo Y, Sunami S, Kamitani T, Kawanami S, Setoguchi T, et al. Detection of non-palpable breast cancer in asymptomatic women by using unenhanced diffusion-weighted and T2-weighted MR imaging: comparison with mammography and dynamic contrast-enhanced MR imaging. Eur Radiol 2011;21:11-7.
PUBMED | CROSSREF

12. Kazama T, Kuroki Y, Kikuchi M, Sato Y, Nagashima T, Miyazawa Y, et al. Diffusion-weighted MRI as an adjunct to mammography in women under 50 years of age: an initial study. J Magn Reson Imaging 2012;36:139-44.
PUBMED | CROSSREF

13. Trimboli RM, Verardi N, Cartia F, Carbonaro LA, Sardanelli F. Breast cancer detection using double reading of unenhanced MRI including T1-weighted, T2-weighted STIR, and diffusion-weighted imaging: a proof of concept study. AJR Am J Roentgenol 2014;203:674-81.
PUBMED | CROSSREF

14. Telegrafo M, Rella L, Stabile Ianora AA, Angelelli G, Moschetta M. Unenhanced breast MRI (STIR, T2-weighted TSE, DWIBS): an accurate and alternative strategy for detecting and differentiating breast lesions. Magn Reson Imaging 2015;33:951-5.
PUBMED | CROSSREF

15. McDonald ES, Hammersley JA, Chou SH, Rahbar H, Scheel JR, Lee CI, et al. Performance of DWI as a rapid unenhanced technique for detecting mammographically occult breast cancer in elevated-risk women with dense breasts. AJR Am J Roentgenol 2016;207:205-16.
PUBMED | CROSSREF

16. Kang JW, Shin HJ, Shin KC, Chae EY, Choi WJ, Cha JH, et al. Unenhanced magnetic resonance screening using fused diffusion-weighted imaging and maximum-intensity projection in patients with a personal history of breast cancer: role of fused DWI for postoperative screening. Breast Cancer Res Treat 2017;165:119-28.
PUBMED | CROSSREF

17. Rotili A, Trimboli RM, Penco S, Pesapane F, Tantrige P, Cassano E, et al. Double reading of diffusion-weighted magnetic resonance imaging for breast cancer detection. Breast Cancer Res Treat 2020;180:111-20.
PUBMED | CROSSREF

18. Ha SM, Chang JM, Lee SH, Kim ES, Kim SY, Cho N, et al. Diffusion-weighted MRI at 3.0 T for detection of occult disease in the contralateral breast in women with newly diagnosed breast cancer. Breast Cancer Res Treat 2020;182:283-97.
PUBMED | CROSSREF

19. Jørgensen KJ, Gøtzsche PC, Kalager M, Zahl PH. Breast cancer screening in Denmark: a cohort study of tumor size and overdiagnosis. Ann Intern Med 2017;166:313-23.
PUBMED | CROSSREF

20. Pinker K, Moy L, Sutton EJ, Mann RM, Weber M, Thakur SB, et al. Diffusion-weighted imaging with apparent diffusion coefficient mapping for breast cancer detection as a stand-alone parameter: comparison with dynamic contrast-enhanced and multiparametric magnetic resonance imaging. Invest Radiol 2018;53:587-95.
PUBMED | CROSSREF

21. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA, Bassett LW, Böhm-Vélez M, et al. ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. 5th ed. Reston (VA): American College of Radiology; 2013.

22. IBIS (International Breast Cancer Intervention Study). Online Tyrer-Cuzick model breast cancer risk evaluation tool, IBIS risk assessment tool v8.0b. https://ibis.ikonopedia.com/. Accessed October 3rd, 2020.

23. Baltzer P, Mann RM, Iima M, Sigmund EE, Clauser P, Gilbert FJ, et al. Diffusion-weighted imaging of the breast-a consensus and mission statement from the EUSOBI International Breast Diffusion-Weighted Imaging working group. Eur Radiol 2020;30:1436-50.
PUBMED | CROSSREF

24. Lee SH, Shin HJ, Moon WK. Diffusion-weighted magnetic resonance imaging of the breast: standardization of image acquisition and interpretation. Korean J Radiol 2021;22:9-22.
PUBMED | CROSSREF

25. Riedl CC, Luft N, Bernhart C, Weber M, Bernathova M, Tea MK, et al. Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasound regardless of patient mutation status, age, and breast density. J Clin Oncol 2015;33:1128-35.
PUBMED | CROSSREF

26. Leithner D, Moy L, Morris EA, Marino MA, Helbich TH, Pinker K. Abbreviated MRI of the breast: does it provide value? J Magn Reson Imaging 2019;49:e85-100.
    PUBMED | CROSSREF

27. Partridge SC, Nissan N, Rahbar H, Kitsch AE, Sigmund EE. Diffusion-weighted breast MRI: clinical applications and emerging techniques. J Magn Reson Imaging 2017;45:337-55.
    PUBMED | CROSSREF

28. Newitt DC, Zhang Z, Gibbs JE, Partridge SC, Chenevert TL, Rosen MA, et al. Test-retest repeatability and reproducibility of ADC measures by breast DWI: results from the ACRIN 6698 trial. J Magn Reson Imaging 2019;49:1617-28.
    PUBMED | CROSSREF

29. Welch HG, Prorok PC, O'Malley AJ, Kramer BS. Breast-cancer tumor size, overdiagnosis, and mammography screening effectiveness. N Engl J Med 2016;375:1438-47.
    PUBMED | CROSSREF

30. Greenwood HI, Wilmes LJ, Kelil T, Joe BN. Role of breast MRI in the evaluation and detection of DCIS: opportunities and challenges. J Magn Reson Imaging 2020;52:697-709.
    PUBMED | CROSSREF