Clinical Study

Oncology

Oncology 2012;82:98–107
DOI: 10.1159/000335958

Received: October 5, 2011
Accepted after revision: December 7, 2011
Published online: February 11, 2012

Breast Cancers Detected by Breast MRI Screening and Ultrasound in Asymptomatic Asian Women: 8 Years of Experience in Taiwan

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Key Words
Breast cancer · MRI · Mammography · Screening · US-guided biopsy

Abstract
Background: This study investigated one-stop breast screening combining magnetic resonance imaging (MRI) and ultrasound (US) in asymptomatic Asian women. ***Methods:*** 3,586 asymptomatic women (mean age, 45.3 years) were retrospectively analyzed by breast MRI followed by US. US-guided biopsy was performed when the MRI-detected lesion was confirmed by US. When the lesion was not detected on the initial US, a second-look US guided by MRI findings was performed. Then biopsy was done. MRI-positive and US-negative patients were followed up according to MRI lesion size, MRI lesion morphology, and mammographic diagnosis. ***Results:*** In total, 115 subjects had suspicious malignant lesions and received US-guided biopsy, and 47 malignant lesions, including 35 invasive cancers and 12 carcinoma in situ (CIS) lesions, were diagnosed. More than half (22/35, 63%) of the women with invasive cancer were <50 years of age, and 27 (57.4%) of the 47 cancer cases had early breast cancers. Two invasive cancers (5.7%) and 7 CIS lesions (58.3%) were found at the second-look US. The overall cancer incidence was 1.31% (47/3,586) and increased to 2.2% (78/3,586) if precancerous lesions were included. Subjects aged 41–50 years had the highest incidence of cancer detection (1.97%). Five MRI and US-negative cases had cancers found 1 year after the screening. ***Conclusions:*** The results from the one-stop breast screening in this study showed that combining MRI and US is an efficient multimodality tool for screening asymptomatic Asian women in a metropolitan area of Taiwan who had concerns about the diagnosis and radiation of mammography.

Introduction

The benefit of early detection of breast cancer has been shown in mammographic studies. It was demonstrated that a 25–35% reduction in breast cancer deaths for women aged 50–69 years who undergo screening can be achieved [1]. Although mammography is the most commonly used imaging modality for screening breast can-

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cer, its effectiveness may be reduced in women with dense breasts. In the general population, mammography misses about 22% of invasive cancers in women <50 years of age, compared to 10% in women >50 years [2]. The limitation of mammography testing has led to interest in alternative methods for screening high-risk women to enable early detection of cancer.

Magnetic resonance imaging (MRI) has proven its promise in the detection of asymptomatic or occult breast lesions with high sensitivity [3–5]. MRI also provides valuable information for detecting multicentric breast cancer in women with dense breasts [6]. In March 2007, the American Cancer Society issued a new guideline recommending annual screening for high-risk women using breast MRI. MRI is recommended as an adjunct to mammography for women with a lifetime risk of 20–25% or greater [7]. For women with a 15–20% lifetime risk, based on the analysis of multiple risk factors such as a personal history of breast cancer, carcinoma in situ (CIS), atypical hyperplasia, and extremely dense breasts on mammography, the American Cancer Society suggested that screening decisions should be made on a case-by-case basis [7]. MRI is not recommended because it is associated with substantial numbers of false-positive results and high costs. MRI as a screening tool for breast cancer, however, involves complex factors such as cancer epidemiology, socioeconomic situation, healthcare policy, and awareness and compliance of the general population.

Breast cancer has the highest cancer incidence rate and the fourth highest mortality rate for women in Taiwan [8]. In 1995, Taiwan implemented the universal National Health Insurance Legislation, and >98% of the population are covered [9]. To reduce breast cancer mortality and spread, the Department of Health of Taiwan has initiated a nationwide Taiwan Mammography Screening Program. Effective since July 2004, the program ensures free mammogram service every 2 years for Taiwanese women between 50 and 69 years of age. However, due to patient concerns about radiation exposure and accuracy of mammography, alternative imaging modalities, such as MRI, are demanded to assess the physical situation of asymptomatic women.

While several large studies of MRI for screening women at high risk of breast cancer have recently reported their findings [10–12], there has been no report to our knowledge of the value of breast MRI in evaluating asymptomatic healthy women of moderate risk with dense breasts. In this study, we reported the results of one-stop breast MRI screening at our imaging center. The main goal of the study was to report the clinical experience of using combined MRI and ultrasound (US) for screening healthy Asian women, and not to evaluate the accuracy of breast MRI.

Subjects and Methods

Subjects

From October 2000 to December 2008, 3,681 asymptomatic women underwent breast screening with MRI at our imaging center. Of these 3,681 women, 95 were known to have a prior history of cancer and were excluded from the study. The remaining breast MRI scans from 3,586 women (mean age, 45.3 years) were retrospectively analyzed. All subjects came to our imaging center for breast screening with MRI by self-referral; most were introduced by families or friends who had been receiving MRI studies at our center. Since our institution prohibits advertisement, we did not recruit subjects for the screening program. Diagnostic breast MRI studies for women with palpable lumps, suspicious breast lesions found in other hospitals, or with diagnosed breast cancer, and/or women coming for a second opinion were excluded.

MRI Studies

All subjects were examined with a 1.5-tesla scanner (Siemens Medical Solutions, Erlangen, Germany). A circularly polarized, two-channel breast-dedicated surface coil was used to receive the signal. The MRI protocol included high temporal resolution dynamic contrast-enhanced study (3D FLASH T1WI) for kinetic analysis and high spatial resolution images (3D FLASH T1WI) for morphological assessment. All the images were acquired in the axial plane. The imaging parameters were: TR/TE = 16/6.9 ms; slice thickness = 1.0–1.5 mm; field of view = 32 cm, and voxel size = 0.80–0.89 × 0.63 × 1.0–1.2 mm for the dynamic study. The total scanning time was about 2 min for the dynamic T1WI and 4 min for the high spatial resolution image. Additionally, a T2WI was included in the scanning protocol to detect fibrocystic or cystic lesions (scanning time was 3 min 45 s). The total examination of the whole set of breast MRI scans, including positioning and scanning, took about 25 min.

Interpretation of MRI Scans

All MR images were viewed by one of five board-certified radiologists, who had 4–19 years of experience in interpreting breast MRI (average, 9.6 years). The imaging interpretation was based on the criteria of the American College of Radiology (ACR) Breast Imaging Reporting and Database System (BI-RADS) lexicon [13]. The ACR BI-RADS MRI lexicon includes two major categories of descriptors: morphology and enhancement kinetics. Imaging features suspicious of a malignant lesion in MRI included an enhanced mass lesion with spiculated or irregular margins, a non-mass-like enhancement lesion with clumped or ductal enhancement, or an enhanced lesion showing a time-intensity curve of fast initial enhancement and washout pattern, or a fast initial enhancement and plateau pattern.

Complementary US Study

US examination was performed for each individual on the same day of the breast MRI to provide tissue characterization and guidance for needle biopsy when needed. The US examinations were

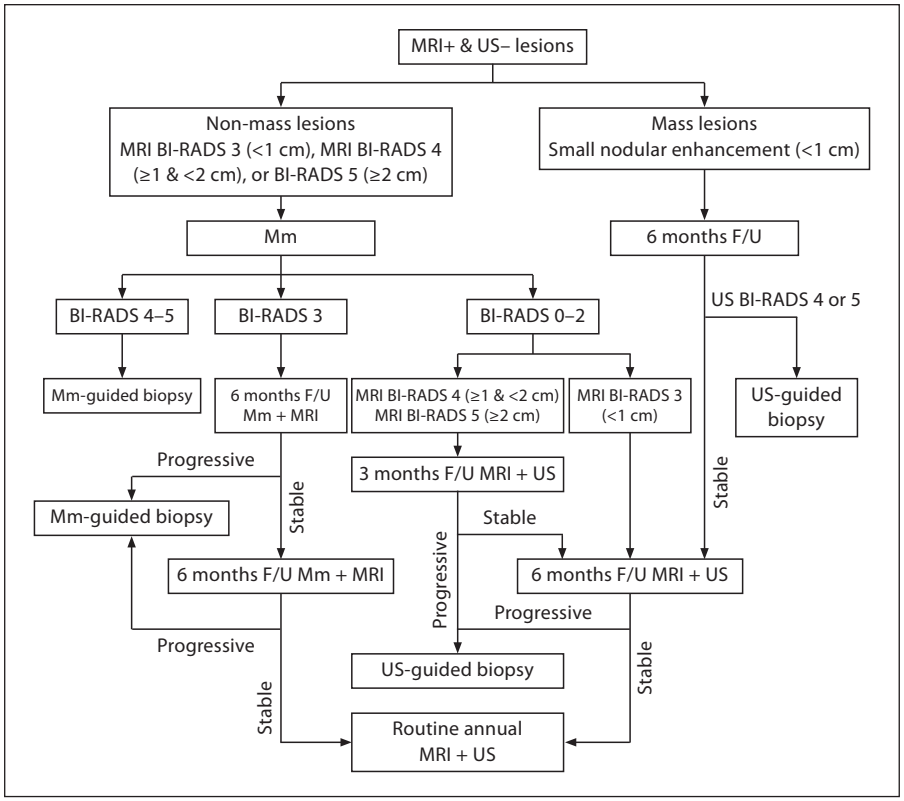

Fig. 1. Flowchart of the further diagnostic procedures for women showing positive MRI and negative US findings. Mm = Mammography; F/U = follow-up. MRI BI-RADS 3 (<1 cm): MRI appearance is BI-RADS 3 in any size or non-mass lesion <1 cm; MRI BI-RADS 4 (≥1 & < 2 cm): MRI appearance is BI-RADS 4 in any size or non-mass lesion size 1–2 cm; MRI BI-RADS 5 (≥2 cm): MRI appearance is BI-RADS 5 in any size or non-mass lesion size ≥2 cm.

whole-breast screening studies, not merely limited to the evaluation of the abnormal MRI-detected area. US was performed by board-certified radiographers. The results were reviewed and confirmed by the same radiologist who interpreted the MRI. Therefore, the US studies were not blind to the MRI findings. The imaging interpretation was based on the ACR BI-RADS US lexicon. The MRI and US findings were carefully compared and correlated. If the MRI-detected lesion was also seen in US, immediate fine needle aspiration cytology and/or core needle biopsy were performed under US guidance. If suspicious lesions were detected on MRI but showed negative results on initial US, targeted US guided by MRI findings was immediately performed by the same radiologist.

When a cancer or precancerous lesion was diagnosed, the examinees received standard care, including tumor staging and appropriate treatment. Follow-up mammograms were also performed selectively in some women with biopsy-proven malignancy.

Management for MRI-Positive but US-Negative Patients

If an MRI-suspected lesion was not detected in the target US, the subject was sent for mammographic study. Patients were managed in different ways according to MRI lesion size and morphology, and mammographic diagnosis. Figure 1 is a flowchart showing how this category of patients was managed. For example, for highly suspicious (BI-RADS 5) or large (>2 cm) ductal CIS (DCIS)-like lesions found in MRI, if mammography showed positive findings or BI-RADS category 4 or 5 lesions, the patient was referred to the breast clinic for mammography-guided biopsy. If mammography showed negative findings, the patient was followed up by MRI and US.

Results

Mammographic Studies after MRI and US

Mammography was not routinely performed at our imaging center. For some women with proven cancer (by US-guided biopsy), mammography was, however, arranged by clinical doctors when they were referred to a breast clinic. Mammograms were obtained for 20 of the 35 cases of invasive cancer and all 12 cases of the CIS group. According to the ACR BI-RADS categories, 13 of the 20 (65%) cases of invasive cancer had suspicious findings or needed additional imaging evaluation (3 cases were BI-RADS category 4, 5 were category 5 and 5 were category 0) in mammography. The other 7 cases (35%) had negative findings (fig. 2). Seven of the 12 mammograms (58.3%) of the CIS group had suspicious findings or needed additional imaging evaluation (3 cases were BI-RADS category 4, 2 were category 5 and 2 were category 0); 5 (41.7%) were negative or had benign findings (2 cases were category 1 and 3 were category 2).

Lesion Types and Cancer Incidence

Overall, 115 of the 3,586 subjects were suspected to have malignant lesions in both breast MRI and US; US-

guided biopsy (n = 106) and/or aspiration cytology study (n = 122) was performed in all 115 subjects. Of the whole cohort, none of the women received mammography-guided biopsy. Forty-seven women, 25 (53%) premenopausal and 22 (47%) postmenopausal women, were proven to have malignant lesions in pathology. Three of the 47 women had family histories of breast cancer. Family history was taken from the patients themselves directly. In this study, we have already excluded patients who came to our MRI center with a history of breast cancer. After confirmation of breast cancer, patients were referred to a breast surgeon for further evaluation and treatment. Of these 47 cancers, 35 were invasive (fig. 3) and 12 were CIS. Their age ranged from 33 to 71 years, with a mean age of 47.5 years in the invasive cancer group and 52.7 years in the CIS group. Seventeen of the 35 patients with invasive cancer (17/35, 49%) and none (0%) of the CIS patients showed clinically palpable lesions when retrospectively examined by the clinicians at our imaging center after their MRI studies. These 17 women did not feel the lesion by themselves. The MRI-assessed tumor size for these 17 patients ranged from 0.5 to 4.0 cm (mean 2.3 cm).

In the invasive cancer group, 2 cases (5.7%) were found at second-look US (fig. 4, 5) after acquiring the lesion map on MRI. In the CIS group, 7 cases (58.3%) could not be identified on the initial US. With the help of MRI findings, however, second-look US identified those 7 cases well. Two women showed malignancy in both breasts: 1 showed bilateral invasive ductal cancer and the other showed invasive cancer in one breast, and DCIS and lobular CIS in the other.

The most common cellular type of invasive cancer was ductal carcinoma (27/35, 77.1%), followed by lobular carcinoma (7/35, 20%), and 1 case of apocrine carcinoma (1/35, 2.9%). In the CIS group, all cases were of the ductal type (12/12, 100%). Additionally, 31 cases of precancerous lesions (13 cases of epithelial hyperplasia with cellular atypia, 15 cases of papilloma, and 3 cases of phyllode tumor) were diagnosed. The incidence of malignancy in our asymptomatic screening cohort was 1.31% (47/3,586) and 2.2% (78/3,586) if all precancerous lesions were included. Table 1 shows the number of CIS lesions and invasive cancers in the different age groups: cancer incidence showed two peaks. Screening in subjects aged 41–50 years resulted in the highest incidence of cancer detection (27/1,373, 1.97%), including 6 in situ lesions and 21 invasive cancers. Subjects aged 61–70 years were the second peak (7/397, 1.76%). The cancer incidence was much higher in women aged 41–50 years than in those 51–60 years (1.97 vs. 0.80%).

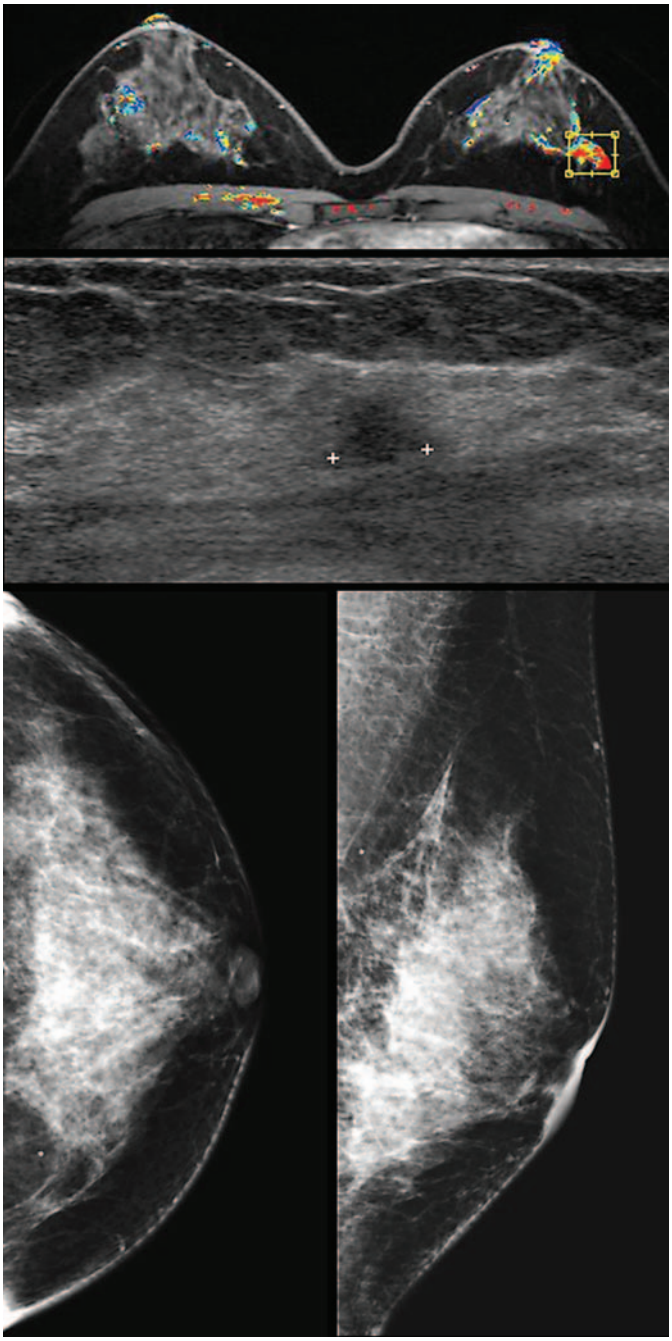

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Fig. 2. A 44-year-old woman showing a heterogeneously enhanced mass lesion in the left breast by MRI and a hypoechoic lesion with irregular margins by US. US-guided biopsy confirmed an invasive lobular cancer. Follow-up mammography at the breast clinic did not show any abnormalities.

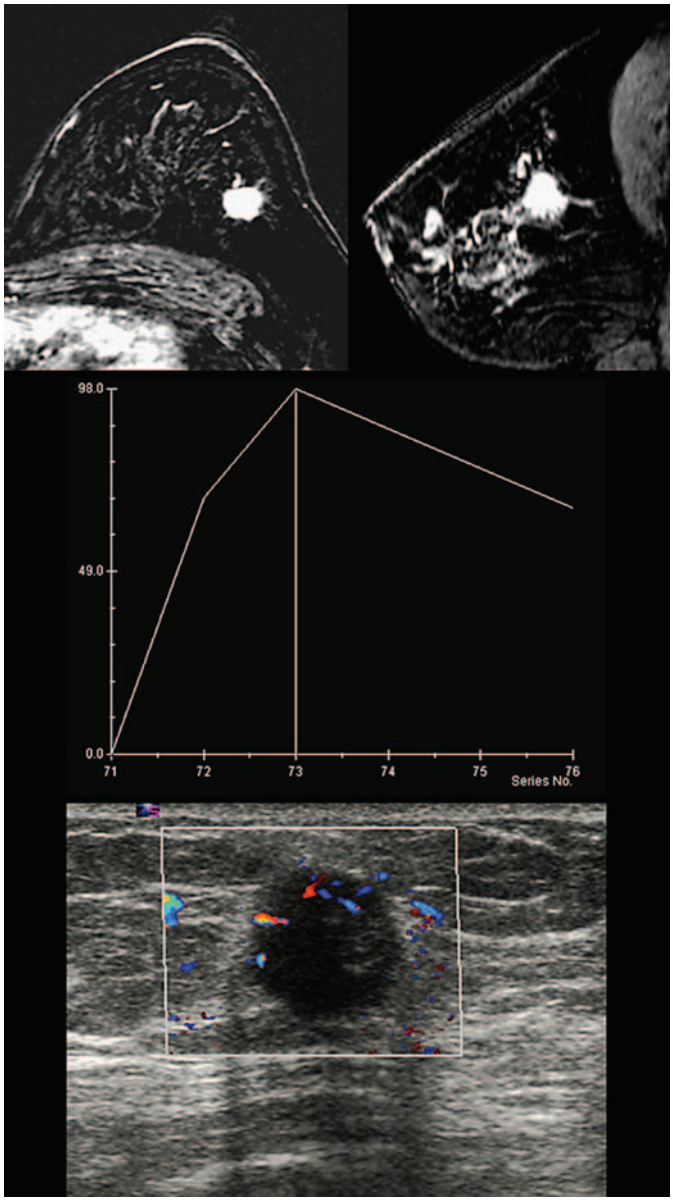

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Fig. 3. A 33-year-old woman showing a well-enhanced mass lesion in the left breast by MRI. The image in the sagittal section demonstrates a spiculated margin (a malignant sign) in the lesion. Kinetic enhancement curve shows a rapid wash-in and -out pattern, another typical malignant characteristic. US examination shows a well-defined hypoechoic lesion with remarkable tumor angiogenesis. US-guided biopsy proved it was an invasive ductal cancer.

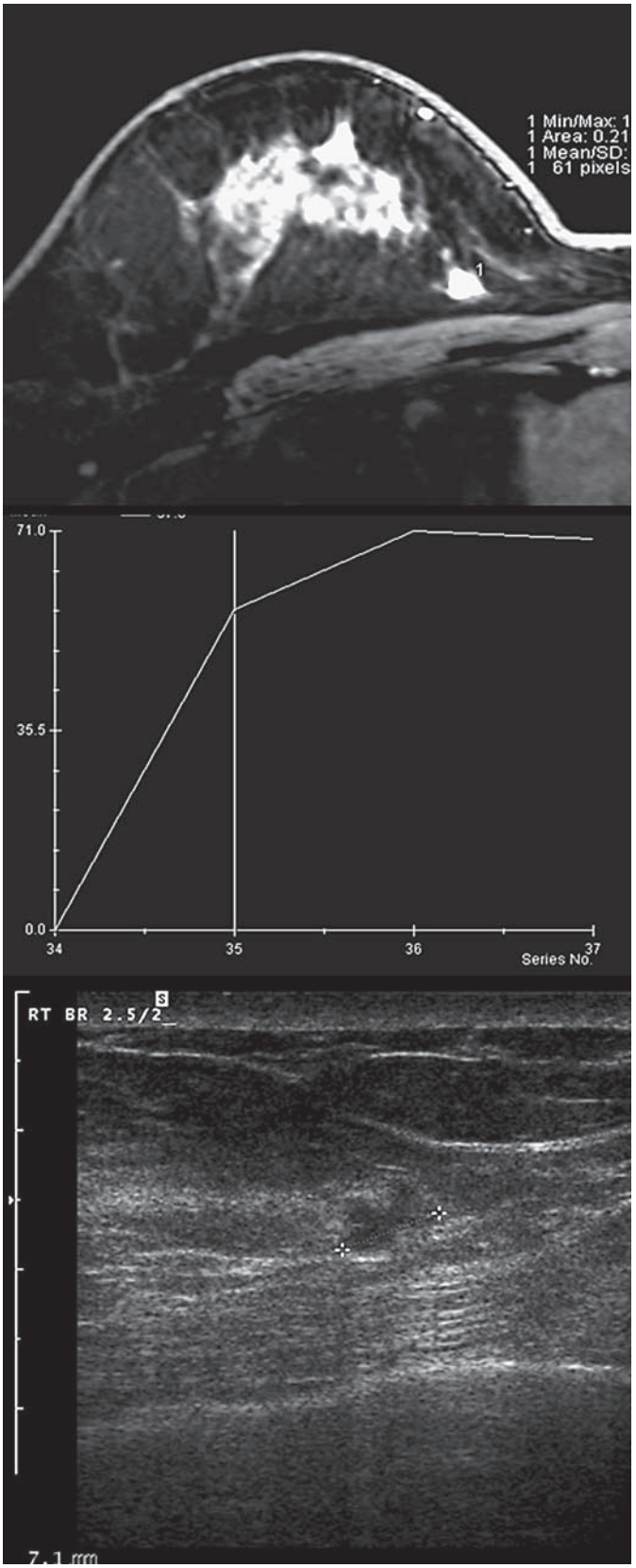

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Fig. 4. A 33-year-old woman with an irregular mass lesion with strong enhancement in the right breast by MRI. Kinetic enhancement curve shows a rapid wash-in and plateau pattern (suspicious of malignancy). Initial US examination did not find any suspicious lesions. The second-look US, however, found a hypoechoic lesion with irregular margins in the junction of the glandular tissue and fatty lobules. The tumor was about 7 mm. US-guided biopsy confirmed an invasive ductal cancer.

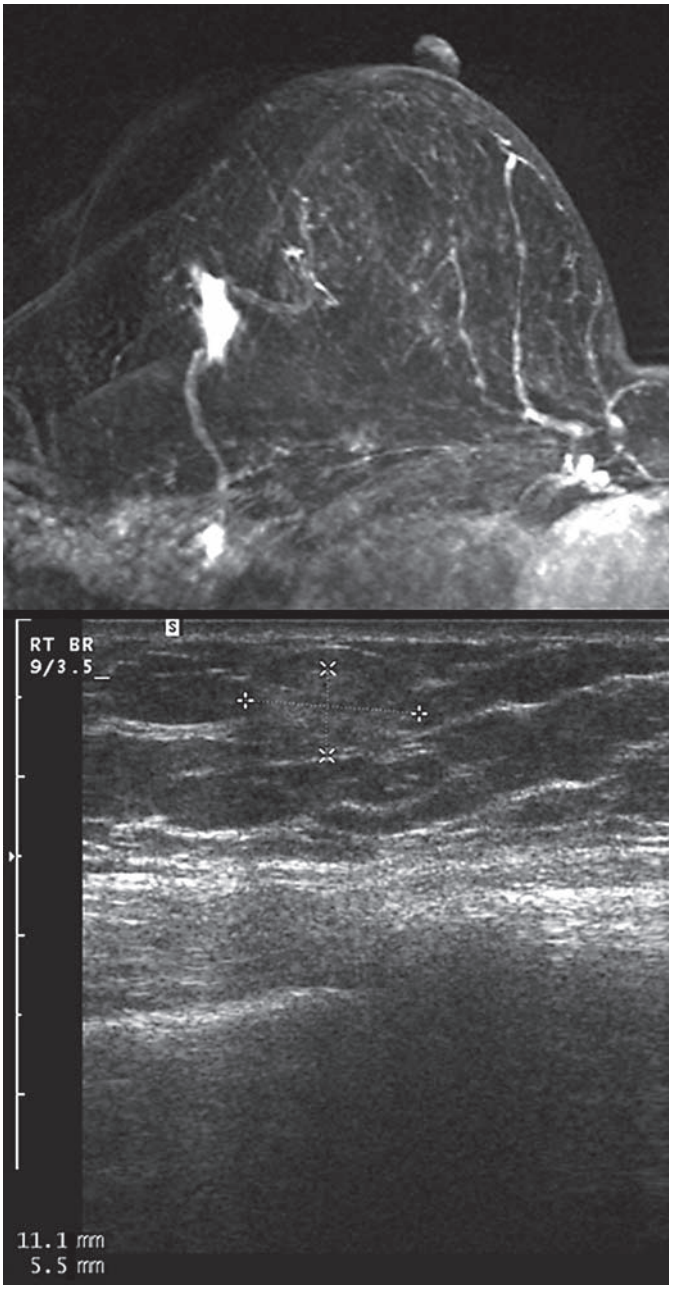

Fig. 5. A 56-year-old woman with an irregular mass lesion with strong enhancement in the right breast by MRI. Initial US examination did not find any suspicious lesions. The second-look US, however, found an iso-echoic lesion with irregular margins located inside the fat lobules. The tumor was about 11.1 × 5.5 mm. US-guided biopsy proved it was an invasive lobular cancer.

Table 1. Breast cancer diagnosed by age group

Age group	Examinees n	CIS		Invasive cancer	
		n	%	n	%
11–20 years	4	0	0.00	0	0.00
21–30 years	115	0	0.00	0	0.00
31–40 years	586	0	0.00	4	0.68
41–50 years	1,373	6	0.44	21	1.53
51–60 years	1,007	4	0.40	4	0.40
61–70 years	397	2	0.50	5	1.26
71–80 years	99	0	0.00	1	1.01
81–90 years	5	0	0.00	0	0.00
Total	3,586	12	0.33	35	0.98

Of the 47 cancer cases, more than half (27/47, 57.4%) had early breast cancer (stage 0 & I): 12 cases of TNM stage 0 disease (25.5%), 15 of stage I disease (31.9%), 13 of stage IIa (27.7%), 2 of stage IIb (4.3%), 1 of stage IIIa (2.1%) and 4 of stage IV disease (8.5%). The mean tumor size for invasive cancer was 1.8 cm (median, 1.8 cm, range 0.3–4.5 cm) and for CIS it was 1.2 cm (median, 0.9 cm, range 0.5–2.2 cm). Tables 2 and 3 present the clinical and imaging data and management of the 35 patients with invasive cancer and the 12 with CIS, respectively. Of the subjects without cancer at initial screening, 4 cases were found to have breast cancer 1 year later, 3 at our imaging center and 1 at another hospital; in 1 case, breast cancer was detected 2 years later at our imaging center. None of these 5 cases were found to have suspicious lesions in their previous MRI (1–2 years ago).

Discussion

The incidence of invasive breast cancer in women has been rapidly increasing in Asia [14, 15]. A study [16] found that the prevalence of tumor subtypes differed between Taiwanese patients and Caucasians and African Americans. Mammographic screening had a significant effect on the decrease in breast cancer. Nevertheless, recommendations for breast cancer screening with imaging have become increasingly complex [17]. Non-mammographic screening methods, particularly MRI, and, recently, breast US, have supplemented mammography to compensate for the limitations of mammographic screening [10, 12, 18–21]. In this study, mammography was not routinely included for all women and, therefore, may be considered as 'not a standard of

Table 2. Clinical and imaging data for the 35 women with invasive cancer

Case No.	Age	Clinical exam (palpable)	Family history	Menstrual status	MRI	US	Mm BI-RADS	BC in Mm	Pathology	Tumor size, cm	Tumor staging	Lesion side	Treatment
1	40	+	–	pre	+	+	N/A	N/A	IDC	2.2	IIA (T2N0M0)	RT	MRM
2	43	+	–	pre	+	+	N/A	N/A	IDC	3.5	IIB (T2N1M0)	RT	MRM
3	50	–	–	post	+	+	5	3	IDC	1.2	I (T1N0M0)	LT	BCS
4	43	+	–	pre	+	+	N/A	N/A	IDC	0.5	I (T1N0M0)	LT	BCS
5	47	+	–	pre	+	+	N/A	N/A	IDC	3	IIA (T2N0M0)	RT	MRM
6	49	– –	–	post	+ +	+ +	N/A	N/A	IDC	4.5 (LT) 1.7 (RT)	IV (multiorgan metastases)	BIL	C/T
7	44	+	–	pre	+	+	0	4	ILC	2.5	IIA (T2N0M0)	LT	MRM
8	46	–	–	pre	+	+	0	3	IDC	0.5	I (T1N0M0)	LT	BCS-A
9	43	+ for LT axillary LAP – for breasts	–	pre	+ +	+ +	5	3	LT: IDC RT: DCIS + LCIS	0.7 (LT) 2.0 (RT)	IIA (T1N1M0)	BIL	NAC + BCS-A for LT
10	33	–	–	pre	+	2nd look	4	4	IDC	0.4	IIIA (T1N2M0)	LT	MRM
11	44	+	–	pre	+	+	0	3	ILC	3	IIA (T2N0M0)	LT	BCS-A
12	47	+	–	pre	+	+	N/A	N/A	IDC	2.3	IIA (T2N0M0)	LT	BCS-A
13	56	–	–	post	+	2nd look	N/A	N/A	ILC	2	I (T1N0M0)	RT	MRM
14	34	–	–	pre	+	+	1	3	ILC	0.6	I (T1N0M0)	LT	BCS
15	67	–	–	post	+	+	0	3	IDC	1.3	I (T1N0M0)	RT	MRM
16	42	–	–	pre	+	+	N/A	N/A	IDC	0.8	I (T1N0M0)	LT	BCS-A
17	46	–	–	pre	+	+	5	3	IDC	1.5	IIA (T1N1M0)	RT	BCS
18	44	+	+ mom	pre	+	+	N/A	N/A	IDC	4	IV (bone metastasis)	LT	C/T + R/T
19	54	+	–	post	+	+	1	3	ILC	1.5	I (T1N0M0)	RT	MRM
20	67	+	–	post	+	+	0	3	apocrine carcinoma	2.5	IIA (T2N0M0)	LT	MRM
21	52	+	–	post	+	+	N/A	N/A		1.5	I (T1N0M0)	LT	TCM
22	42	–	–	pre	+	+	1	3	IDC	0.6	I (T1N0M0)	LT	BCS
23	42	–	–	pre	+	+	1	3	IDC	2.1	IIA (T2N0M0)	RT	MRM
24	61	–	–	post	+	+	N/A	N/A	IDC	1	IIA (T1N1M0)	RT	MRM
25	50	–	–	post	+	+	N/A	N/A	IDC	0.7	I (T1N0M0)	RT	BCS-A
26	62	–	–	post	+	+	N/A	N/A	IDC	2	IV (multiorgan metastases)	RT	N/A
27	53	–	–	post	+	+	5	3	IDC	1.8	I (T1N0M0)	LT	BCS-A
28	47	–	+ mom	pre	+	+	1	3	IDC	1.8	IIA (T1N1M0)	LT	BCS
29	44	+	–	pre	+	+	1	4	ILC	0.9	I (T1N0M0)	LT	MRM
30	65	+	–	post	+	+	5	1	IDC	3.3	IIA (T2N0M0)	LT	MRM
31	46	–	–	pre	+	+	N/A	N/A	IDC	2.9	IIA (T2N1M0)	LT	MRM
32	71	+	–	post	+	+	4	2	ILC	3	IIB (T2N1M0)	RT	SM
33	33	+	–	pre	+	+	4	3	IDC	1.7	I (T1N0M0)	RT	SM
34	45	+	–	pre	+	+	N/A	N/A	IDC	2.2	IV (T2N2M1)	LT	NAC + MRM
35	50	–	–	post	+	+	1	3	IDC	0.3	I (T1N0M0)	RT	SM

The clinical examination was performed by the clinicians at our imaging center after the breast MRI (retrospective palpation). Mm = Mammography; BC = breast composition; N/A = not assessed or no treatment; RT = right; LT = left; BIL = bilateral; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; MRM = modified radical mastectomy with axillary lymph node dissection; BCS = breast-conserving surgery with sentinel lymph node sampling; BCS-A = breast-conserving surgery with axillary lymph node dissection; TCM = traditional Chinese medical treatment; SM = simple mastectomy with axillary lymph node dissection; LAP = lymphadenopathy; NAC = neoadjuvant chemotherapy; C/T = chemotherapy; R/T = radiotherapy; mom = mother.

care'. However, currently there is a trend in Taiwan that MRI, rather than mammography, is being used as the major screening tool for women who have concerns regarding radiation exposure and can afford to have a breast MRI study.

The major benefits of breast MRI are its high sensitivity in detecting breast carcinoma and its ability to depict cancers that are occult on mammography, US, and clinical breast examination [22]. In women with dense breasts, breast MRI was significantly superior to both mammog-

Table 3. Clinical and imaging data for the 12 women with CIS

Case No.	Age	Clinical exam (palpable)	Family history	Menstrual status	MRI	US	Mm BI-RADS	BC in Mm	Pathology	Tumor size, cm	Tumor staging	Lesion side	Treatment
1	63	–	–	post	+	2nd look	4	3	DCIS	0.8	0	LT	PM
2	45	–	–	pre	+	+	5	3	DCIS	2.2	0	RT	SM
3	49	–	–	pre	+	2nd look	1	3	DCIS	0.5	0	LT	PM
4	60	–	–	post	+	+	2	3	DCIS	0.5	0	LT	PM
5	56	–	–	post	+	2nd look	1	3	DCIS	0.7	0	LT	PM
6	64	–	–	post	+	+	4	3	DCIS	2.1	0	LT	SM
7	52	–	–	post	+	2nd look	2	3	DCIS	0.9	0	LT	BCS
8	46	–	–	pre	+	2nd look	2	3	DCIS	0.9	0	RT	BCS
9	47	–	–	pre	+	+	5	3	DCIS	2	0	RT	BCS
10	49	–	–	post	+	+	0	4	DCIS	1.5	0	LT	BCS
11	53	–	–	post	+	2nd look	4	3	DCIS	2.2	0	RT	SM
12	48	–	+ mom	post	+	2nd look	0	3	DCIS	0.7	0	RT	PM

The clinical examination was performed by the clinicians at our imaging center after the breast MRI (retrospective palpation). Mm = Mammography; BC = breast composition; LT = left; RT = right; PM = partial mastectomy; BCS = breast-conserving surgery with sentinel lymph node sampling; SM = simple mastectomy with axillary lymph node dissection; mom = mother.

raphy and US in terms of diagnostic accuracy [23]. Breast MRI, however, has its limitations, e.g. false-positive findings and higher costs than mammography and US. The current American Cancer Society guidelines [7] also state that there is insufficient evidence for MRI to be recommended as a routine examination for women with extremely dense breasts, despite several reports on the value of breast MRI in this subgroup of women [6, 24–26].

In Taiwan, the first peak of breast cancer is in women aged 40–50 years (before menopause), and most women have dense breasts. Many look for MRI studies at their own costs. In this study, the MRI center was located in a metropolitan area. The socioeconomic status of our subjects was most likely in the top one third of the whole society. Since cost was not a consideration for these women, and most Taiwanese women have dense breasts that will decrease the sensitivity of mammography, we used a top-down rather than bottom-up approach.

The regular clinical setting takes long before the diagnosis of breast cancer is confirmed in asymptomatic patients. At our imaging center, we provide a one-stop service. We did MRI and US at the same visit. Adjunct US was used to minimize false-positive results of MRI and also for US-guided biopsy if indicated. The accuracy of breast US is unaffected by breast density. US has therefore been applied to 'screen' women with dense breast tissue [27–30]. The cytology report was available within 1 h. If the suspicious lesion was proven to be a benign one, then the stress on the patient was immediately relieved. If the suspicious lesion was malignant, the staging was evaluated at the same time using whole-body MRI. These patients were referred to breast surgeons without any further diagnostic workup. The ultrashort equivocal period from diagnosis to staging, usually less than half a day, most efficiently reduced the stress. It was found that 51% of the participants screened were very anxious at every stage of the prediagnostic phase [31]. Waiting for additional investigation and test results is characterized by concerns and fear, and is a very distressing period for most women [32, 33]. The one-stop service initiated at our imaging center in Taiwan has gained popularity in the past years, and now many imaging centers are providing the same service.

In this study, the cancer incidence at our asymptomatic screening cohort was 1.3%. Literature reports of the number of cancers detected per MRI screening range from 1% for the Dutch study [10] to 1.8% for the MARIBS study [12], to 4.8% for the Canadian study [11]. In a prospective cohort study of multimodality screening of 609 high-risk women [34], 20 cancers were diagnosed in 18 patients. The overall cancer yield on a per-patient basis was 3.0%. In a study [35] comprising 209 breast MRI scans carried out in 171 asymptomatic patients, 7 cancers were detected, with a yield of 4.1%. Only 1 of the 7 cancers was also shown by mammography. In another MRI study [36] of women screened with a family history of breast cancer, cancer was detected in 9/374 patients (2%). Of the 9 cancer

patients, 7 cancers were detected by MRI only. The different cancer detection rates across different studies may be due to different cancer risks in the study cohorts and differences in the multimodality imaging methods used.

In our study, of the 35 women diagnosed with invasive cancer, 22 (63%) were <50 years of age. Of the 47 cancer cases, 27 (57.4%) had early breast cancer. In a prospective multicenter cohort study of 687 women [37] with an elevated family risk of breast cancer, 27 women were diagnosed with breast cancer: 11 DCIS (41%) and 16 invasive cancers (59%). It was concluded that in women with elevated familial risk, quality-assured MRI screening shifts the distribution of screen-detected breast cancers toward the preinvasive stage. Two of the 35 women with invasive cancers (5.7%) and 7 of the 12 women with CIS (58.3%) were detected by second-look US guided by MRI findings. It was therefore quite important to have MRI to overcome the operator dependence of US. The information provided by second-look US may help in further clinical decision making [38, 39]. If the MRI-detected lesion is seen on US, biopsy may be performed under US rather than MRI guidance [38]. Compared with MRI, US is less expensive, more readily available, and more comfortable for the patient.

Of the 35 women with invasive cancer, 20 women also received mammography studies at the breast clinic. Seven of these 20 cases (35%) had negative or benign findings. A meta-analysis of five MRI studies as an adjunct to conventional imaging in high-risk women has provided convincing evidence that MRI detects additional cancers, with an incremental sensitivity of 58% (95% CI, 47–70%) compared with mammography alone [11, 12, 18–20, 40]. In conjunction with conventional mammography, the sensitivity of MRI as a screening tool has been reported to be 93–100% [12, 24, 41]. Of the 12 MRI-detected CIS lesions, 5 lesions (41.7%) showed negative or benign findings in mammograms due to the absence of microcalcifications. This result contradicts earlier studies that suggested MRI to be substantially less sensitive than mammography specifically regarding DCIS [10, 12]. A prospective observational study [42] has shown that MRI examination was superior to mammography for DCIS detection, with 56% diagnosed by mammography and 92% by MRI ($p < 0.0001$). In the EVA cohort [37], half of the invasive cancers (8 of 16) and more than half of the DCIS (6 of 11) were only detected by MRI. MRI might be even more valuable for detecting in situ lesions in most of the Asian women with dense breasts, for which mammography may not be sensitive enough. Nevertheless, so far, there is no randomized trial showing that MRI is better than mammography.

This study has several limitations. MRI is a more expensive diagnostic tool than mammography. Even though our top-down approach has attracted many women in a metropolitan area, women with a lower socioeconomic background in rural areas may not be able to afford MRI screening. We did not collect the detailed clinical data of MRI-positive and US-negative cases. Since many of the patients with MRI-suspected lesions did not have biopsies due to the lack of an MRI-guided biopsy device at our imaging center, the diagnostic performance of MRI could not be accurately evaluated. All of the subjects followed up were, however, stable, and none received US- or mammography-guided biopsy in the following year. A number of asymptomatic women did not detect a palpable breast lesion detected as abnormality by a clinician subsequently. The inclusion of these women in the screening study is equivocal. Since several radiologists interpreted breast MRI and performed US examinations, inter-operator variation may affect the diagnosis of MRI presented in this study. We did not provide the service of MRI-guided biopsy. However, US was carried out immediately after MRI for correlation and, if necessary, US-guided biopsy could be performed.

In summary, one-stop breast MRI with adjunct US at our imaging center has proven that the screening procedure is efficient for asymptomatic women in Taiwan. More than half of the cancers were found in women <50 years and were in early stage. The cancer incidence was within the range of published reports for screening high-risk women. Despite the current debate on how to perform breast cancer screening, one important consensus is that the decision should be made based on individualized assessment of the breast cancer risk. The results from our study suggested that for most Asian women with dense breasts, an accurate and affordable multimodality screening tool should be actively searched. Healthcare policies regarding the screening for young asymptomatic women should be seriously investigated and initiated.

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