Clinicopathological Characteristics of Lesions Diagnosed by MRI-Guided Biopsy in *BRCA1/2* Mutation Carriers

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ABSTRACT

Objective: *BRCA1/2* pathogenic variant carriers face a high risk of breast cancer, making early detection vital for minimizing systemic treatments. Contrast-enhanced magnetic resonance imaging (MRI) outperforms mammography and ultrasound in detecting lesions that are often missed, particularly in individuals with *BRCA1* or *BRCA2* variants. However, the effectiveness of MRI-guided biopsy remains unclear. Thus, the aim was to evaluate the effectiveness of MRI-guided biopsy in detecting malignancy among *BRCA1/2* pathogenic variant carriers with MRI-only-detected breast lesions and compare these findings with those in non-carriers and assess lesion characteristics and diagnostic yield.

Materials and Methods: We retrospectively analyzed. We compared the effectiveness of MRI-guided biopsy for *BRCA1/2* pathogenic variant carriers with MRI-only-detected lesions with that of non-carriers between April 2018 and December 2022. We examined the clinicopathological characteristics and MRI findings of the *BRCA1/2* carriers.

Results: A total of 130 lesions from 126 patients were reviewed. The *BRCA1/2* mutation group had a significantly higher incidence of category 3 lesions on MRI. Invasive carcinoma was more prevalent among *BRCA1/2* carriers, and non-carriers predominantly presented with ductal carcinoma *in situ*. MRI-guided biopsy identified malignant tumors in 30.1% of lesions. The positive predictive values were 42.9% for *BRCA1/2* carriers and 28.6% for non-carriers.

Conclusion: MRI-guided biopsy was effective in detecting early-stage invasive carcinoma in *BRCA1/2* carriers, highlighting its role in tailored surveillance strategies. For new lesions categorized as breast imaging reporting and data system 3 on MRI, biopsy should be considered, particularly for *BRCA1/2* carriers. Prospective studies are needed to validate these findings and assess long-term clinical outcomes to inform personalized management approaches for high-risk populations.

Keywords: Breast cancer; magnetic resonance imaging; image-guided biopsy; *BRCA1* gene; *BRCA2* gene; mutation

KEY POINTS

- Features of magnetic resonance imaging (MRI)-guided biopsies in *BRCA1/2* variant carriers and non-carriers differ.
- Pathogenic variant carriers had invasive cancer; non-carriers had non-invasive cancer.
- MRI-guided biopsy helps detect breast cancer early in *BRCA1/2* mutation carriers.

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Introduction

BRCA1/2 pathogenic variants are associated with a high incidence of breast cancer (1, 2). The detection of breast cancer at an early stage in this population is important to avoid the need for systemic treatment. Contrast-enhanced breast magnetic resonance imaging (MRI) has demonstrated significant advantages in identifying suspected breast cancer lesions that mammography or ultrasound (US) cannot detect (MRI-only detected lesions) in *BRCA1/2* pathogenic variant carriers (3). Both the Japanese and National Comprehensive Cancer Network guidelines for the diagnosis and treatment of hereditary breast and ovarian cancers (HBOC) recommend annual surveillance using contrast-enhanced breast MRI for *BRCA1/2* pathogenic variant carriers who have already developed breast or non-breast cancers (4, 5).

Since April 2020, the Japanese National Insurance scheme has covered breast cancer surveillance using contrast-enhanced breast MRI for *BRCA1/2* pathogenic variant carriers who have developed breast or ovarian cancer. Furthermore, MRI-guided biopsy of lesions detected has been covered by the Japanese National Insurance System since April 2018. However, the availability of this procedure remains limited in facilities. Owing to the scarcity of reports on MRI-guided biopsy findings, the indications and appropriate management of this procedure to avoid unnecessary biopsies have not been well established (6-9).

In this study, we evaluated the utility of MRI-guided biopsy in *BRCA1/2* pathogenic variant carriers with MRI-only detected lesions, compared to non-carriers.

Materials and Methods

Patients and Methods

Patients with and without *BRCA1/2* pathogenic variants who underwent MRI-guided biopsy between April 2018 and December 2022 were included in this study. All patients underwent both mammography and US; cases in which lesions were detected on MRI-targeted US following MRI were excluded.

For *BRCA1/2* pathogenic variant-positive cases, all MRI examinations performed for surveillance were scheduled according to the menstrual cycle. In contrast, MRI examinations performed for preoperative staging did not follow the menstrual cycle, and in some cases, the procedure was halted during biopsy due to a lack of reproducibility.

All the breast MRI images were evaluated by two radiologists who had 25 (M.T.) and 15 years of experience with breast MRI. Lesions were categorized as focus, mass, or non-mass enhancement (NME) according to the breast imaging reporting and data system (BI-RADS) 5th edition of the American College of Radiology (10). For

mass lesions, the lesion shape (oval, round, or irregular), margin [circumscribed or non-circumscribed (irregular or spiculated)], and internal enhancement characteristics (homogeneous, heterogeneous, rim enhancement, or dark internal septations) were evaluated, based on BI-RADS for MRI. For NME lesions, distribution (focal, linear, segmental, regional, multiple regions, or diffuse), and the internal enhancement pattern (heterogeneous, homogeneous, clumped, or clustered ring) were evaluated, again based on BI-RADS for MRI. An additional evaluation was performed for the internal enhancement pattern (linear ductal or branching). Linear ductal was defined as enhancement arrayed in a single line, and branching was defined as a line that branches, previously described by Tozaki and Fukuda (11) and Machida et al. (12).

For mass lesions, the intralesional regions of interests (ROIs) were drawn using SYNAPSE VINCENT (Fujifilm Medical, Tokyo, Japan). A circular ROI was placed in the target lesion, and a kinetic curve assessment was performed, based on BI-RADS for MRI. A circular ROI larger than 3 pixels was placed on the most suspicious region of the enhancement within a mass lesion. Suspicious regions were defined as areas that exhibit a washout in the delayed phase or a rapid rise in the early phase and were usually located at the margin of the tumor. Fatty tissue and non-enhancing areas in the mass lesion were avoided. The kinetic curve assessment was not performed for focus and NME lesions because it is difficult to set the ROI and reproducibility is not guaranteed. The classification for focus, mass, and NME lesions was based on the categories reported by Tozaki and Fukuma (13), with some modifications (Table 1).

We compared the clinicopathological characteristics, MRI findings, and pathological features of *BRCA1/2* pathogenic variant carriers (*BRCA1/2* group) to those of non-carriers (non-carrier group). Sensitivity and positive predictive values were used to assess the accuracy of MRI-guided biopsy for MRI-only detected lesions in *BRCA1/2* pathogenic variant carriers compared with non-carriers. The association between MRI and pathological findings was also examined. This retrospective study was approved by the Ethics Review Board of Showa University (approval no: 2023-033-B, date: February 25, 2025). Informed consent was obtained in the form of an opt-out on our website.

MRI Technique

A breast MRI was performed using a 1.5-T system (Signa HDx Ver. 16; GE Healthcare, Milwaukee, WI, USA). All the patients were examined in the prone position using a dedicated 8-channel breast coil. Before contrast material administration, transverse T1-weighted (TR/TE, 6.1/3; flip angle, 12°; field of view, 20 cm; matrix, 320×192; slice thickness, 2.4 mm; time of acquisition, 158 s) and transverse fat-suppressed T2-weighted fast spin-echo (TR/TE, 3060/102: field of view, 35 cm; matrix size, 320×256; slice

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Table 1. Categorization of breast lesions on contrast-enhanced MRI

Breast lesion type and BI-RADS MRI category	Findings on contrast-enhanced MRI
Mass lesion	
Category 5	Spiculated margin
	Irregular lesion: fast washout pattern and rim enhancement
Category 4B/C	Irregular lesion
	Circumscribed margin: washout pattern
Category 4A	Circumscribed margin: non-washout and initial fast rise
Category 3	Circumscribed margin: neither washout nor initial fast rise
Focus lesion	
Category 4A	Not circumscribed margin
Category 3	Circumscribed margin
Non-mass lesion	
Category 5	Segmental distribution and clustered ring enhancement
Category 4B/C	Segmental distribution
	Clustered ring enhancement
	Clumped architecture
	Brancing ductal pattern
Category 4A	Linear ductal pattern
Category 3	Not showing the characteristics of category 4 or 5

BI-RADS: Breast imaging reporting and data system, MRI: Magnetic resonance imaging

thickness, 2.0 mm: time of acquisition, 86 seconds) sequences were performed. Axial diffusion-weighted echo-planar imaging along the x-y-z axes (TR/TE, 5850/85 ms; field of view, 38 cm; matrix, 128×128; slice thickness, 5.0 mm; b-values of 0 and 1500 s/mm^2) was also performed.

Dynamic MRI using a three-dimensional (3D) fat-suppressed volume imaging breast assessment (VIBRANT) sequence with parallel acquisition was obtained before and three times after a bolus injection of Gd-DOTA (0.1 mmol/kg at a rate of 0.8 mL/s), followed by a 60-mL saline flush using an automatic injector. Both breasts were examined in the transverse plane using the first-, second-, and third-phase dynamic images acquired at 30 seconds, 1.5 minutes, and 4.5 minutes, respectively. The dynamic MRI parameters were: TR/TE, 6.1/3.0; flip angle, 12°; field of view, 20 cm; matrix, 320×192; interpolated slice thickness, 2.4 mm; and time of acquisition, 71 seconds. The right and left breasts were examined in the sagittal plane using the VIBRANT sequence without parallel acquisition at 2.5 and 3.5 minutes (between the second- and third-phase images), respectively (TR/TE, 4.2/1.6; flip angle, 12°; field of view, 23 cm; matrix, 320×192; interpolated slice thickness, 2 mm; time of acquisition, 60 seconds).

MRI-Biopsy Procedure

All biopsies were performed by radiologists specializing in breast imaging. A vacuum-assisted breast biopsy unit using a 10-gauge breast biopsy system (EnCor Enspire™ breast biopsy system, Becton, Dickinson and Company, NJ, USA) or a 9-gauge breast biopsy system (ATEC® Breast Biopsy System, Hologic, Inc., Marlborough, MA, USA) was used. The procedure consisted of the following steps.

1. Compression Plate and Marker Placement

A grid-type compression plate was used. Two markers (vitamin E capsule) were placed in the block near the predicted puncture site. A grid and markers were drawn on a transparent sheet, and the sheet was fixed on the monitor of the workstation, with reference to a sagittal image. The scale of enlargement was adjusted to make the size of the blocks on the monitor screen the same as that of the blocks on the sheet.

2. Contrast-Enhanced MRI

MRI was performed before and after intravenous injection of 10 mL of Gd-DOTA. Transverse and sagittal 3D-VIBRANT sequences with fat suppression (TR/TE 5.6/2.7 or 4.0/1.5; flip angle 12°; field of view 20 or 23 cm; matrix 320×192; slice thickness 1 mm; time of acquisition 60–71s) were obtained.

3. Estimation of the Puncture Site

The target lesion was confirmed by contrast-enhanced MRI. The puncture site was detected according to the positional relationships between the grid line, markers, and the lesion on the sagittal image. The depth was measured on the transverse image, as the distance from the skin to the lesion.

4. Sterilization and Anesthesia

The skin within the block to be punctured was sterilized. After an anesthetic was injected into the subcutaneous tissue and around the lesion, an incision of about 4 mm was made in the skin, and an introducer was inserted.

5. Insertion of the Introducer

The introducer was inserted so as to set the lesion at the center of the opening of the vacuum-assisted biopsy (VAB) needle. After the introducer was inserted into the target site, the block was fixed moderately, and the introducer was removed. Then, an obturator was inserted into the introducer cannula, and images were obtained for confirmation.

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6. Insertion of the VAB Needle: Tissue Sampling

After confirming that the lesion was set at the appropriate position, the obturator was removed, and the VAB needle was inserted. After obtaining several samples, the obturator was inserted again, and images were obtained again for confirmation. Additional tissue sampling was performed as needed. After the tissue sampling was completed, in many of the cases, markers [UltraClip Dual Trigger Breast Tissue Marker; BD (C.R. Bard, Inc.), Tempe, AZ, or TriMark® Biopsy Site Marker; Hologic, Inc., Marlborough, MA, USA] were retained in the breast.

Statistical Analysis

We analyzed complete-case data comprising *BRCA1/2* pathogenic variant carriers lesions and non-carrier lesions. For the primary binary outcomes, we computed risk ratios (RR), risk differences (RD), and odds ratios (OR) with 95% confidence intervals (CIs) from 2×2 tables. The RR CIs were derived on the log scale and exponentiated back to the RR scale. Holm-Bonferroni correction was applied for primary comparisons, and two-tailed tests with $\alpha = 0.05$ were set. Analyses were conducted in R 4.5.2; the full analysis script is available in the supplementary materials.

Results

A total of 130 lesions from 126 patients were retrospectively analyzed. The clinicopathological characteristics of the 130 lesions are presented in Table 2. All patients were female, with a median (range) age of 50 (25–82) years. Four patients had multiple lesions. The *BRCA1/2* group accounted for 12.3% (16/130) of the lesions, with six patients carrying *BRCA1* and ten carrying *BRCA2*, including one with a variant of uncertain significance and "uncertain/risk may be increased" (Case 7, see Table 3).

MRI Findings

Based on the lesion shapes detected on MRI, the rate of NME was significantly lower in the *BRCA1/2* mutation group (38%) than in the non-carrier group (64%) ($p = 0.04$). The 130 lesions were categorized as follows: category 3, 10 lesions (7.7%); category 4, 117 lesions (90%); and category 5, three lesions (2.3%). The *BRCA1/2* group had a significantly higher rate of category 3 cases (25%, 4/16) undergoing MRI-guided biopsy than the non-carrier group (5.3%, 6/114) ($p = 0.006$). Among the *BRCA genes*, 5 out of 6 *BRCA1* and 7 out of 10 *BRCA2* cases detected by MRI were diagnosed as category 4 (Table 3).

Integrated Statistics (MRI Findings)

The comparisons between *BRCA1/2* carriers and non-carriers showed a statistically significant difference in both the rate of NME and the distribution of categories. Specifically, *BRCA1/2* carriers had a lower rate of NME (38%) compared with non-carriers (64%), with a *p*-value adjusted for multiple comparisons

Table 2. Clinicopathological characteristics of the MRI-detected lesions

			Total n (%)	*BRCA1/2* n (%)	Others n (%)	p
Lesion			130	16 (12)	114 (88)	
Age	Mean (range)		50 (25–82)	50 (32–71)	50 (25–82)	0.19
Cancellation of MRI biopsy			4 (3.1)	2 (13)	2 (1.8)	
MRI findings	Lesion type	Focus	10 (7.7)	4 (25)	6 (5.3)	0.04*
		Mass	41 (32)	6 (38)	35 (31)	
		NME	79 (61)	6 (38)	73 (64)	
	BI-RADS category	Category 3	10 (7.7)	4 (25)	6 (5.3)	0.01
		Category 4	117 (90)	12 (75)	105 (92)	
		Category 5	3 (2.3)	0	3 (2.6)	
Pathological findings	Malignant		38 (30)	6 (43)	32 (29)	0.33**
	Indeterminate		5 (4.0)	0	5 (4.5)	
	Benign		83 (66)	8 (57)	75 (67)	
	Histological type		38	6	32	
	Invasive (IDC, ILC)		12 (32)	5 (83)	7 (22)	0.00***
	DCIS		25 (66)	1 (17)	24 (75)	
	LCIS		1 (2.6)	0	1 (3.1)	

*: Comparison between focus+mass and NME, **: Comparison between malignant and benign, except for indeterminate, ***: Comparison between invasive cancer and DCIS+LCIS. NME: Non-mass enhancement; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; DCIS: Ductal carcinoma *in situ*; LCIS: Lobular carcinoma *in situ*; MRI: Magnetic resonance imaging; BRCA: Breast cancer; BI-RADS: Breast imaging reporting and data system

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(*p*_adj) below 0.05. In addition, *BRCA1/2* carriers exhibited a higher proportion of category 3 lesions (25%) relative to non-carriers (5.3%), also reaching *p*_adj<0.05. The category 3 outcome indicated that *BRCA1/2* carriers had 0.67 times the risk of category 3 lesions compared with non-carriers (RR = 0.67; 95% CI, 0.18–0.76; RD = -0.23; OR = 0.37; *p*_adj<0.05). For lesions with NME, *BRCA1/2* carriers had 0.66 times the risk of NME compared with non-carriers (RR = 0.66; 95% CI, 0.37–1.16; RD = -0.29; OR = 0.54; *p*_adj<0.05).

MRI-Guided Biopsy

The annual number of MRI-guided biopsy cases from 2019-2022 was 30, 18, 24, and 43, respectively (median 27) giving a *BRCA1/2* pathogenic variant-positive rate of about 5% per year. MRI-guided biopsy was discontinued during the examination of four lesions: two in the *BRCA1/2* group and two in the non-carrier group. Consequently, MRI-guided biopsy was performed for 126 lesions: 14 in the *BRCA1/2* group and 112 in the non-carrier group from

No	Age	BRCA	Menopausal	Purpose	Lesion type	Size (mm)	Kinetic curve assessment	BI-RADS category	Pathological findings on biopsy	Pathological findings on surgical specimen/ size
1	52	*BRCA1*	RRSO	Surveillance	Focus	4		3*	IDC, TNBC, Ki-67 30–40%	Scar/0 mm
2	37	*BRCA1* unexposed	Pre	Surveillance	Mass	5	Fast-washout	4	IDC, TNBC, Ki-67 60–70%	DCIS, luminal A-like, Ki-67 60–70%/1mm
3	48	*BRCA1*	Post	Surveillance	Mass	5	Fast-washout	4	Benign	
4	33	*BRCA1* unexposed	Pre	Surveillance	Mass	7	Fast-persistent	4	Benign	
5	32	*BRCA1*	Pre	Surveillance	NME	15		4	Cancellation	
6	32	*BRCA1*	Pre	Staging	NME	8		4	Cancellation	
7	55	*BRCA2*	RRSO	Surveillance	Mass	5	Fast-persistent	4	IDC, luminal A-like, Ki-67 10-20%	IDC/0.5 mm
8	49	*BRCA2*	Pre	Surveillance	Mass	12	Fast-plateau	4	IDC, luminal B-ike, Ki-67 40–50%	IDC/3 mm
9	67	*BRCA2*	Post	Staging	NME	8		4	IDC, TNBC, Ki-67 10–20%	pCR
10	67	*BRCA2*	RRSO	Surveillance	NME	14		4	DCIS, luminal A-like, Ki-67 10–20%	DCIS, luminal A-like, Ki-67 <5%/1 mm
11	55	*BRCA2* VUS	Post	Surveillance	Focus	4		3*	Indeterminate, atypical lobular hyperplasia	Follow-up
12	50	*BRCA2*	RRSO	Surveillance	Focus	3		3*	Benign	
13	55	*BRCA2*	Unknown	Surveillance	Focus	4		3*	Benign	
14	33	*BRCA2*	Pre	Surveillance	Mass	7	Fast-washout	4	Benign	
15	71	*BRCA2*	Post	Staging	NME	14		4	Benign	
16	56	*BRCA2*	Post	Staging	NME	11		4	Benign	

*: New lesions detected during follow-up period. RRSO: Risk-reducing salpingo-oophorectomy; NME, Non-mass enhancement; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; DCIS: Ductal carcinoma *in situ*; TNBC: Triple negative breast cancer; pCR: Pathologic complete response, BRCA: Breast cancer; BI-RADS: Breast imaging reporting and data system; VUS: Variant of uncertain significance

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2018-2022. Malignant tumors were pathologically diagnosed in 38 of the 126 biopsied lesions (30.1%). The sensitivity for detecting malignant tumors did not differ significantly between *BRCA1/2* carriers (37.5%, 6/16) and non-carriers (28.1%, 32/114) ($p = 0.56$). Positive predictive values were 42.9% (6/14) in the *BRCA1/2* group and 28.6% (32/112) in the non-carrier group. The positive predictive values according to BI-RADS categorization were 10% (1/10) for category 3, 35% (39/113) for category 4, and 100% (3/3) for category 5. Among the four cases in which the examination was discontinued, three were in their 30s, and two were in their early 30s among the *BRCA1* cases. In one *BRCA1* case, a lesion was noted on the surveillance MRI, and the subsequent MRI performed within two years showed no significant changes. Biopsy was performed in the latter half of the menstrual cycle when background parenchymal enhancement (BPE) was strong. In the other case, a lesion was identified using MRI for staging purposes before surgery, but it had disappeared by the time of biopsy. MRI for staging was performed in the latter half of the menstrual cycle; however, the biopsy was performed seven days after the onset of menstruation, when the effects of BPE were at their weakest. The disappeared lesion did not reappear on subsequent MRI scans during the 2-year follow-up period.

Pathological Findings

Of the 38 pathologically malignant tumors detected by MRI-guided biopsy, invasive carcinoma (including invasive ductal carcinoma and invasive lobular carcinoma) was diagnosed

in 12 of 126 biopsied lesions (9.5%). This included 5 of the 14 lesions in the *BRCA1/2* group (35.7%) and 7 of the 112 lesions in the non-carrier group (6.2%). Two of the five were *BRCA1* variants, and three were *BRCA2* variants, with the two *BRCA1* variants diagnosed as invasive triple-negative breast cancer. The detection rate of invasive carcinoma using MRI-guided biopsy was significantly higher in the *BRCA1/2* group than in the non-carrier group ($p = 0.003$). Ductal carcinoma *in situ* (DCIS) was diagnosed in 25 lesions (19.8%): one in the *BRCA1/2* group (7.1%) and 24 in the non-carrier group (21.4%) (Figures 1 and 2).

Integrated Statistics (Pathological Findings)

Invasive cancer among biopsied lesions is more prevalent in *BRCA1/2* carriers, with 5 of 16 lesions showing invasive cancer compared with 7 of 114 in the non-carrier group, yielding a relative risk of 2.29, a RD of 0.17, and an OR of 3.52 (95% CI, 1.11–11.20; p_adj <0.05).

Discussion and Conclusion

The objective of our study was to assess the efficacy of MRI-guided biopsy in identifying breast cancer in *BRCA1/2* pathogenic variant carriers compared to non-carriers. MRI-guided biopsy detected malignant tumors in 30.1% of the studied lesions, with a higher detection rate in *BRCA1/2* pathogenic variant carriers (42.9%) than in non-carriers (28.6%). Furthermore, the higher detection rate of invasive carcinoma by MRI-guided biopsy in *BRCA1/2* carriers compared to non-carriers is a novel finding.
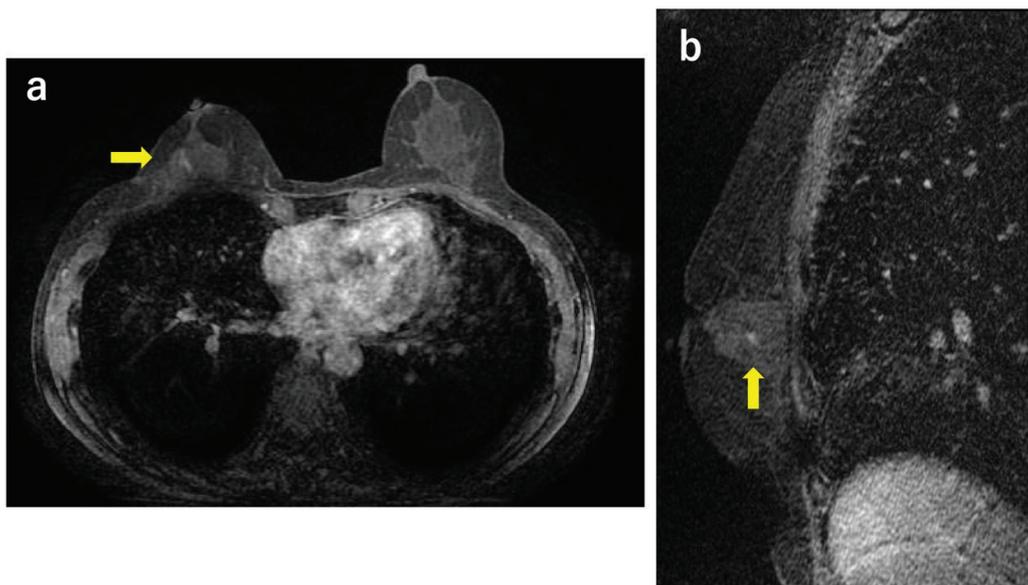

Figure 1. (a, b) case 10: a 67-year-old woman, a *BRCA2* pathogenic variant carrier, developed peritoneal cancer eight years after surgery and risk-reducing salpingo-oophorectomy for right ductal carcinoma *in situ*. She received chemotherapy, and subsequent magnetic resonance imaging (MRI) surveillance showed a category 4 non-mass enhancement with branching in the right outer quadrant. MRI-guided biopsy diagnosed ductal carcinoma *in situ*. The patient underwent right and contralateral prophylactic mastectomies
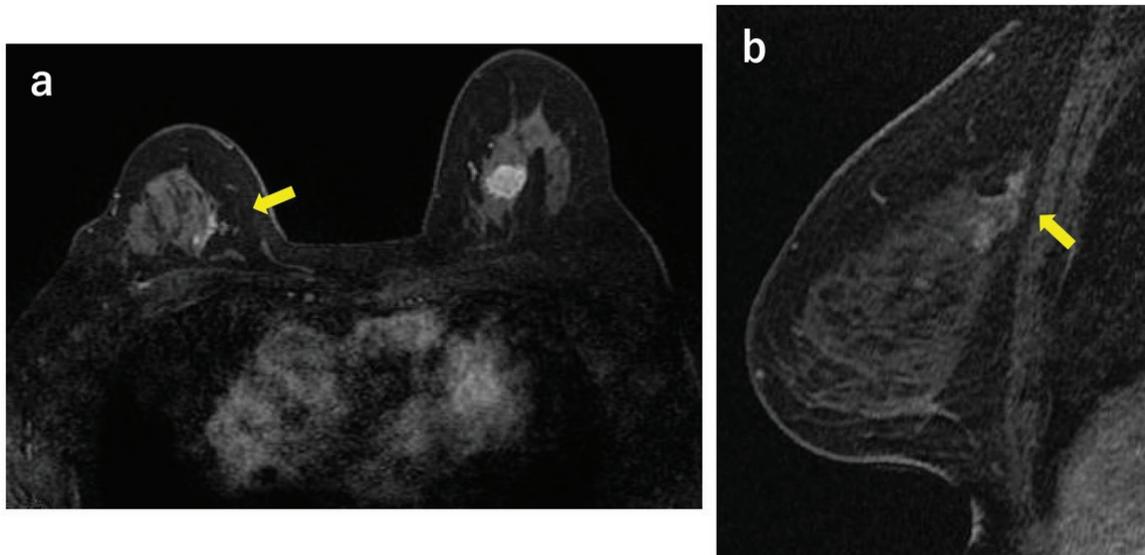
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Figure 2. (a, b) case 9: a 67-year-old woman, a *BRCA2* pathogenic variant carrier, was diagnosed with left breast cancer (T2N0, triple-negative breast cancer) 17 years after right breast-conserving surgery and sentinel node biopsy with preoperative chemotherapy for right breast cancer. Preoperative staging magnetic resonance imaging (MRI) revealed category 4 non-mass enhancement with branching in the right inner upper quadrant. MRI-guided biopsy identified triple-negative invasive ductal carcinoma. She was diagnosed with in-breast recurrence in the conserved right breast. Bilateral surgery was performed after preoperative chemotherapy

Early detection of breast cancer is particularly beneficial in *BRCA1/2* pathogenic variant carriers because of the higher risk of developing the disease.

Takahama et al. (7) reported that 38% (115 of 301) of lesions subjected to MRI-guided biopsy in Japan were diagnosed with breast cancer. Our findings support this earlier finding and highlight the efficacy of MRI-guided biopsy in detecting breast lesions, particularly in high-risk populations, such as *BRCA1/2* carriers.

The most significant difference in the MRI findings between the *BRCA1/2* and non-carrier groups was the shape of the detected lesion. NME was detected at a significantly lower rate in the *BRCA1/2* mutation group than in the non-carrier group (p = 0.04). This finding may be attributed to the higher prevalence of invasive cancer in the *BRCA1/2* group, in contrast to the 75% of cases in the non-carrier group that presented with DCIS (p = 0.003).

Interestingly, early-stage breast cancer in *BRCA1* pathogenic variant carriers may appear as benign findings, such as cysts and fibroadenomas, based on US findings (14, 15). Case 1, which was diagnosed with malignant C3, was depicted as a focus. Due to the small size of the lesion, evaluating the margins was challenging, and the contrast pattern did not exhibit washout findings, raising suspicion of a fibroepithelial tumor. As this was a new finding, a biopsy was performed, which confirmed the malignant diagnosis.

In addition, it has been reported that *BRCA2* pathogenic variant carriers often show features of intraductal lesions (16, 17). Murakami et al. (16) reported that NME was absent in *BRCA1* pathogenic variant carriers (0/30) and present in 24% (6/25) of *BRCA2* pathogenic variant carriers. In cases diagnosed as malignant, these characteristics were not observed.

Typically, biopsy is indicated for cases of category 4 or higher; however, in this study, four cases in the *BRCA1/2* group were classified as category 3, and one of them was diagnosed as malignant. All four cases had new lesions during MRI surveillance. Considering that all six cases in category 3 of the control group yielded benign results, we believe that MRI-guided biopsy should be considered for new lesions during MRI surveillance for *BRCA1/2* pathogenic variants, even if the imaging findings indicate category 3.

According to the subtype of invasive carcinoma, *BRCA1* variants have a poor prognosis because of rapidly progressing triple-negative breast cancer (18), whereas the luminal type accounts for the majority of *BRCA2* pathogenic variant carriers. However, more than 60% of these cases are regarded as high-risk by multigene assays and may require chemotherapy if the tumor enlarges (19, 20). Thus, the higher detection rate of invasive cancer with worse prognosis in *BRCA1/2* pathogenic variant carriers undergoing MRI-guided biopsy underscores the importance of early detection, intervention, and tailored surveillance strategies for high-risk populations. In our study, chemotherapy was deemed unnecessary for all patients

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because of early tumor removal, which is an advantage of MRI surveillance and MRI-guided biopsy (21). Our findings support the periodic use of MRI for the surveillance of *BRCA1/2* carriers, emphasizing the need for expanded access to this procedure to facilitate timely diagnosis and treatment.

Study Limitations

This study has several limitations that should be considered when interpreting the results. First, the retrospective nature of the study may have resulted in selection bias. Secondly, a relatively small sample size, particularly for *BRCA1/2* carriers, was analyzed. In addition, the lack of long-term follow-up data for benign lesions diagnosed using MRI-guided biopsy limits the assessment of clinical outcomes. Finally, the MRI-guided biopsy was discontinued in some patients in the *BRCA1/2* (13%) and non-carrier (1.8%) groups. *BRCA1* variant carriers were in their early 30s. In general, MRI can exhibit significant variations owing to the menstrual cycle and associated BPE (22-24). Therefore, the optimal imaging time for breast MRI with contrast is 7–14 days after the onset of menstruation (10, 24). *BRCA1/2* pathogenic variant carriers tend to be younger when they develop breast cancer. Performing MRI scans periodically, taking into account the menstrual cycle of *BRCA1/2* pathogenic variant carriers, is warranted to avoid unnecessary biopsies (25).

In conclusion, our study revealed that MRI-guided biopsy can more frequently detect early-stage invasive carcinoma in *BRCA1/2* carriers than in non-carriers. Moreover, periodic MRI follow-up should be recommended for BRCA carriers in high-risk groups, and even newly developing BI-RADS 3 lesions may warrant biopsy to facilitate early diagnosis. Future research prospectively validating our findings in larger cohorts of *BRCA1/2* carriers and non-carriers is needed to assess the clinical outcomes and long-term survival associated with MRI-guided biopsy-detected lesions in this population and to inform personalized management approaches for high-risk populations.

References

1. Noguchi S, Kasugai T, Miki Y, Fukutomi T, Emi M, Nomizu T. Clinicopathologic analysis of BRCA1- or BRCA2-associated hereditary breast carcinoma in Japanese women. Cancer. 1999; 85: 2200-2205. (PMID: 10326698) [Crossref]

2. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol. 2007; 25: 1329-1333. (PMID: 17416853) [Crossref]

3. Peters NH, Borel Rinkes IH, Zuithoff NP, Mali WP, Moons KG, Peeters PH. Meta-analysis of MR imaging in the diagnosis of breast lesions. Radiology. 2008; 246: 116-124. (PMID: 18024435) [Crossref]

4. Japanese Organization of Hereditary Breast and Ovarian Cancer. Guideline for diagnosis and treatment of hereditary breast and ovarian cancer 2021. JOHBOC; 2021. Accessed March 30, 2025. [Crossref]

5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): breast cancer. Version 5.2020. Published May 8, 2023. Accessed March 30, 2025. [Crossref]

6. Tozaki M, Yamashiro N, Sakamoto M, Sakamoto N, Mizuuchi N, Fukuma E. Magnetic resonance-guided vacuum-assisted breast biopsy: results in 100 Japanese women. Jpn J Radiol. 2010; 28: 527-533. (PMID: 20799018) [Crossref]

7. Takahama N, Tozaki M, Ohgiya Y. Current status of MRI-guided vacuum-assisted breast biopsy in Japan. Breast Cancer. 2021; 28: 1188-1194. (PMID: 32632846) [Crossref]

8. Perlet C, Heywang-Kobrunner SH, Heinig A, Sittek H, Casselman J, Anderson I, et al. Magnetic resonance-guided, vacuum-assisted breast biopsy: results from a European multicenter study of 538 lesions. Cancer. 2006; 106: 982-990. (PMID: 16456807) [Crossref]

9. Zebic-Sinkovec M, Hertl K, Kadivec M, Cavlek M, Podobnik G, Snoj M. Outcome of MRI-guided vacuum-assisted breast biopsy - initial experience at Institute of Oncology Ljubljana, Slovenia. Radiol Oncol. 2012; 46: 97-105. (PMID: 23077445) [Crossref]

10. American College of Radiology. ACR breast imaging reporting & data system (BI-RADS). Accessed March 30, 2025. [Crossref]

11. Tozaki M, Fukuda K. High-spatial-resolution MRI of non-masslike breast lesions: interpretation model based on BI-RADS MRI descriptors. AJR Am J Roentgenol. 2006; 187: 330-337. (PMID: 16861534) [Crossref]

12. Machida Y, Tozaki M, Shimauchi A, Yoshida T. Two distinct types of linear distribution in nonmass enhancement at breast mr imaging: difference in positive predictive value between linear and branching patterns. Radiology. 2015; 276: 686-694. (PMID: 25875971) [Crossref]

13. Tozaki M, Fukuma E. 1H MR spectroscopy and diffusion-weighted imaging of the breast: are they useful tools for characterizing breast lesions before biopsy? AJR Am J Roentgenol. 2009; 193: 840-849. (PMID: 19696300) [Crossref]

14. Schrading S, Kuhl CK. Mammographic, US, and MR imaging phenotypes of familial breast cancer. Radiology. 2008; 246: 58-70. (PMID: 18096529) [Crossref]

15. Karbasian N, Sohrabi S, Omofoye TS, Le-Petross H, Arun BK, Albarracin CT, et al. Imaging features of triple negative breast cancer and the effect of BRCA mutations. Curr Probl Diagn Radiol. 2021; 50: 303-307. (PMID: 32033821) [Crossref]

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16. Murakami W, Tozaki M, Nakamura S, Ide Y, Inuzuka M, Hirota Y, et al. The clinical impact of MRI screening for BRCA mutation carriers: the first report in Japan. Breast Cancer. 2019; 26: 552-561. (PMID: 30820924) [Crossref]

17. You C, Xiao Q, Zhu X, Sun Y, Di G, Liu G, et al. The clinicopathological and MRI features of patients with BRCA1/2 mutations in familial breast cancer. Gland Surg. 2021; 10: 262-272. (PMID: 33633982) [Crossref]

18. Foulkes WD. BRCA1 functions as a breast stem cell regulator. J Med Genet. 2004; 41: 1-5. (PMID: 14729816) [Crossref]

19. Halpern N, Sonnenblick A, Uziely B, Divinsky L, Goldberg Y, Hamburger T, et al. Oncotype Dx recurrence score among BRCA1/2 germline mutation carriers with hormone receptors positive breast cancer. Int J Cancer. 2017; 140: 2145-2149. (PMID: 28120435) [Crossref]

20. Ide Y, Liu L, Miura S, Inuzuka M, Akashi-Tanaka S, Sawada T, et al. Frequency of high-risk hormone receptor-positive breast cancer patients was much higher in Japanese breast cancer patients with germline BRCA1/2 mutations than in sporadic breast cancer patients. Breast J. 2021; 27: 188-190. (PMID: 33378795) [Crossref]

21. Saadatmand S, Geuzinge HA, Rutgers EJT, Mann RM, de Roy van Zuidewijn DBW, Zonderland HM, et al; FaMRIsc study group. MRI versus mammography for breast cancer screening in women with familial risk (FaMRIsc): a multicentre, randomised, controlled trial. Lancet Oncol. 2019; 20: 1136-1147. (PMID: 31221620) [Crossref]

22. Kunimatsu N, Kunimatsu A, Uchida Y, Inano S, Nawano S. Factors influencing background parenchymal enhancement on breast MRI classified by mammographic density. KMJ Kitakanto Med J. 2017; 67: 213-220. [Crossref]

23. Kamitani T, Yabuuchi H, Kanemaki Y, Tozaki M, Sonomura T, Mizukoshi W, et al. Effects of menstrual cycle on background parenchymal enhancement and detectability of breast cancer on dynamic contrast-enhanced breast MRI: a multicenter study of an Asian population. Eur J Radiol. 2019; 110: 130-135. [Crossref] Erratum in: Eur J Radiol. 2019; 114: 192. (PMID: 30599849) [Crossref]

24. Kajihara M, Goto M, Hirayama Y, Okunishi S, Kaoku S, Konishi E, et al. Effect of the menstrual cycle on background parenchymal enhancement in breast MR imaging. Magn Reson Med Sci. 2013; 12: 39-45. (PMID: 23474960) [Crossref]

25. Kuhl C, Weigel S, Schrading S, Arand B, Bieling H, König R, et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. J Clin Oncol. 2010; 28: 1450-1457. (PMID: 20177029) [Crossref]