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Epidemiological study of BRCA1 and BRCA2 mutations in a post-nuclear disaster region: A retrospective cohort of 136 breast cancer patients in Fukushima, Japan

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Introduction

Although post-2011 assessments of the Fukushima nuclear accident indicate minimal radiation exposure, it remains important to characterize regional patterns of hereditary breast cancer to establish the epidemiologic baseline needed to evaluate—and, where appropriate, rule out—radiation-related effects. This study aimed to analyze the clinical characteristics of hereditary breast cancer in the area surrounding the Fukushima Daiichi Nuclear Power Station, the site of the 2011 nuclear disaster. This study aimed to determine the prevalence and clinical characteristics of pathogenic *BRCA1/2* variants in 136 breast cancer patients residing in the Hama Dori region of Fukushima Prefecture who underwent *BRCA1/2* testing at a core regional , thereby providing foundational data to inform local medical planning.

Material and Methods

This retrospective observational analysis compared the clinical characteristics of breast cancer patients with and without pathogenic *BRCA* variants. A total of 136 patients diagnosed at the core regional medical institution between July 2020 and December 2024 were included, all of whom met the national insurance eligibility criteria for BRACAnalysis® testing. Clinical variables were assessed between mutation carriers and non-carriers, and specific features of *BRCA*-positive patients were further analyzed.

Results

	BRCA1/2 positive n=25	*BRCA1/2* negative n=111	p-values	Effect sizes	Descriptive statistics
	Average value ± Standard deviation	Average value ± Standard deviation			
age at genetic testing	49±12.2*	50±13.0	0.69	0.09	t-test
residential distance from nuclear power station (km)	45.7±10.2	47.6±7.8	0.30	0.21	t-test
age at radiation exposure	37±12.2	39±12.8	0.44	0.18	t-test
estimated exposure dose (μSv/h)	0.53±0.79	0.69±0.68	0.32	0.21	t-test
age at breast cancer diagnosis	47.0±11.5	49.2±13.0	0.42	0.19	t-test
number of pregnancies	2.3±1.6	2.0±1.3	0.22	0.25	t-test
number of deliveries	1.8±1.4	1.7±1.2	0.75	0.07	t-test
frequency of childbirth at age ≥30 years (%)	13(52)	34(31)	0.07	0.17	Chi-sq
history of breastfeeding (%)	19(76)	78(70)	0.74	0.05	Chi-sq
menopause after age 55 (%)	0(0)	4(4)	-	-	Fisher
alcohol consumption (%)	9(36)	31(28)	0.58	0.07	Chi-sq
smoking history (%)	4(16)	25(23)	0.65	0.06	Chi-sq
Body mass Index at breast cancer diagnosis	24.7±4.7	22.6±5.7	0.08	0.42	t-test

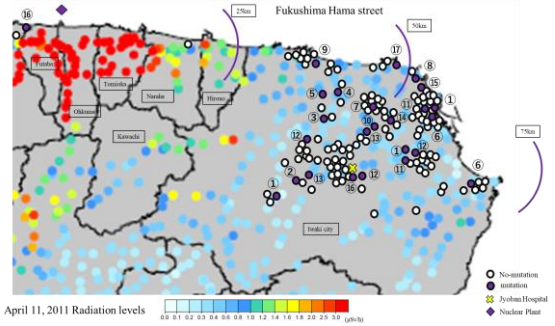
Table 1. Comparison of demographic, reproductive, and lifestyle characteristics by BRCA1/2 pathogenic variant status

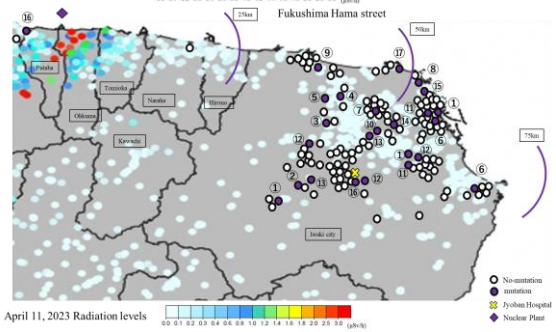
	BRCA1/2 positive n=25	*BRCA1/2* negative n=111	p-values	Effect sizes	Descriptive statistics
Breast cancer stages at the time of genetic testing			0.70	0.13	Chi-sq
0 (%)	1(4)	7(6)			
I (%)	10(40)	45(41)			
II (%)	12(48)	40(23)			
III (%)	1(4)	13(5)			
IV (%)	1(4)	6(6)			
Subtype			0.06	0.18	Fisher
HR+HER2- (%)	16 (64)	89(80)			
HER2+ (%)	2(8)	11(10)			
TNBC (%)	7 (28)	11(10)			
PgR negative (%)	12(48)	22 (20)	0.01	0.25	Chi-sq
Eligibility criteria for insurance-covered *BRCA1/2* testing					
1. breast cancer at age ≤ 45 years (%)	14 (56)	61 (55)	1.00	0.01	Chi-sq
2. two or more primary breast cancers (%)	7 (28)	12 (11)	0.05	0.19	Fisher
3. TNBC diagnosed at age ≤ 60 years (%)	7 (28)	8 (7)	0.01	0.26	Fisher
4. a third-degree relative with a history of breast or ovarian cancer (%)	17 (68)	50 (45)	0.06	0.18	Chi-sq
5. male breast cancer (%)	1 (4)	-	-	-	

Table 2. Comparison of clinical characteristics of breast cancer patients according to *BRCA1/2* pathogenic variant status. HR, hormone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; PgR, progesterone receptor.

	univariable adjusted Poisson regression		multivariable adjusted Poisson regression		VIF
candidate predictors	IRR (95%CI)	p-values	IRR (95%CI)	p-values	
PgR negative	2.77 (1.40-5.48)	0.003	1.89 (0.82-4.34)	0.134	1.60
≥2 primary breast cancers	2.39 (1.16-4.95)	0.018	2.30 (1.23-4.29)	0.009	1.01
TNBC diagnosed at age ≤60	3.14 (1.58-6.25)	0.001	1.93 (0.85-4.36)	0.117	1.60

Table 3. Results of univariable and multivariable adjusted Poisson regression analyses for factors associated with *BRCA1/2* pathogenic variants. IRR, incidence rate ratios; CI, confidence interval; VIF, variance inflation factor; PgR, progesterone receptor; TNBC, triple-negative breast cancer.





BRCA1/2 positive n=25	Patients
***BRCA1* positive n=10**	
1. c.188 T>A (p. Leu63*)	3
2. c.815_824 del (p. Glu272Ala fs*23)	1
3. c.3209 C>A (p. Ala 1070 Glu)	1
4. c.3442 del (p. Glu1148Arg fs*7)	1
5. c.3647 T>G (p. Leu1216*)	1
6. c.5558 A>G (p. Tyr1853Cys)	2
7. del exon 24	1
***BRCA2* positive n=15**	
8. c.475+1 G>A	1
9. c.245_274 delinsGT (p. Lys82Ser fs*5)	1
10.c.1278 del (p. Asp427Thr fs*3)	1
11. c.1813 del (p. Ile605Tyr fs*9)	2
12. c.5576_5579 del (p. ile1859Lys fs*3)	3
13. c.6952 C>T (p. Arg2318*)	2
14. c.7109_7139 dup (p. His2380Gln fs*22)	1
15. c.8504 C>A (p. Ser 2835*)	1
16. c.9076 C>T (p. Gln3026*)	2
17. c.9097 dupA (p. Thr3033Asn fs*11)	1

Table 4. Summary of *BRCA1/2* germline genetic testing results

Discussion and Conclusion

1. This first real-world epidemiologic study from a radiation-affected region of Japan evaluated *BRCA1/2* testing under insurance-based eligibility. National reports show stage distributions of ~9% (0), 40% (I), 39% (II), and 11% (III); molecular subtypes of 68% HR+/HER2–, 6% HER2+, and 24% TNBC; and eligibility triggers of 54% diagnosed at ≤45 years, 18% with ≥2 primaries, 21% TNBC at ≤60, and 52% with a family history. Our cohort closely mirrored these profiles, indicating representativeness of the national BRCA-tested population, and the findings are consistent with the absence of additional radiation-related effects.
2. In our cohort, clinical stage, molecular subtype, and testing eligibility did not differ between *BRCA*-mutated and non-mutated groups, indicating little impact of radiation on breast-cancer phenotype or the germline mutational landscape. Existing evidence does not support radiation-induced *BRCA* mutations from nuclear accidents or medical imaging; nonetheless, because BRCA proteins mediate DNA repair, carriers may be more susceptible to radiation-related carcinogenesis, warranting dose minimization during imaging and treatment. Consistent with this, Chernobyl data show no major differences in breast-cancer incidence or histology by exposure status, and large family-based studies report no excess de novo germline mutations among offspring of exposed individuals. Our findings were consistent with these observations.
3. Taken together, our findings show that *BRCA1/2* testing is feasible and reliable in routine care even in radiation-affected regions, and we found no signal that radiation determines the prevalence or phenotype of hereditary breast cancer. Further studies integrating molecular markers with detailed epidemiology are warranted to clarify gene–environment interactions in breast carcinogenesis.
4. In this Fukushima cohort, pathogenic *BRCA1/2* variants occurred in 18%, comparable to national rates; only having ≥2 primary breast cancers independently predicted *BRCA* positivity. Overall, we found no signal that regional radiation exposure increased the prevalence or altered the phenotype of hereditary breast cancer, and these data provide a local baseline for care and surveillance in this radiation-affected area.

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