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Research article

RISKS OF INCIDENCE OF BREAST CANCER IN A COHORT OF FEMALES OCCUPATIONALLY EXPOSED TO IONIZING RADIATION

A.V. Rumyantseva, T.V. Azizova, M.V. Bannikova

Southern Urals Biophysics Institute, 19 Ozyorskoe shosse, Ozyorsk, 456780, Russian Federation

Breast cancer (BrCa) holds the first rank place in morbidity and mortality due to malignant neoplasms among Russian women.

BrCa is a multifactorial disease and ionizing radiation is among factors that cause elevated risks of developing BrCa.

Our research aim was to assess relative risk (RR) of incidence of BrCa among women who were occupationally exposed to chronic ionizing radiation taking into account radiation and non-radiation factors.

RR of incidence of BrCa was analyzed in a cohort of women employed at a nuclear production enterprise, namely Mayak PA, in 1948–1982. 95 % of women started working at the enterprise at their reproductive age. All those women were chronically exposed to ionizing radiation at their workplaces. A mean cumulative breast absorbed dose of external gamma-ray exposure amounted to 0.45 (standard deviation was 0.68) Gy; an average cumulative muscle absorbed dose of internal alpha-particle exposure amounted to 0.003 (0.01) Gy.

According to data taken from "Clinic" medical-dosimetric database, 165 BrCa cases were detected in 157 women of the analyzed cohort (8 women had BrCa in both breasts).

Our analysis involved calculating RR of incidence of BrCa in relation to known non-radiation and radiation factors. Categorical data analysis was performed without age-related and calendar period-related stratification and with them. RR was analyzed based on Poisson regression with AMFIT module in EPICURE software package.

Incidence of BrCa was revealed to be associated with attained age, age of menarche, age of menopause, number of abortions, age of concomitant diseases prior to cancer diagnosis, height, body mass index, age of hiring at the Mayak PA. There was no relationship between BrCa incidence and cumulative doses of occupational chronic external gamma-ray, internal alpha-particle and neutron exposure.

Keywords: *breast cancer, reproductive health, incidence, risk factors, cohort study, women, long-term occupational radiation exposure, Mayak PA.*

Breast cancer (BrCa) is the most widely spread type of cancer among women in both developed and developing countries [1, 2]. And over the last decades there has been a stable growth in incidence of BrCa in most countries all over the world, the Russian Federation (RF) included. BrCa holds the first place in the morbidity pattern for malignant neoplasms (MNs) in the RF female population (21.1 % in 2017). Incidence of BrCa increased by 22 % among women in the RF over 2007–2017 with average annual growth rates of 2.8 % [3, 4].

BrCa is a multifactorial disease. There are several established factors that cause elevated risks of BrCa including age older than 40 years, early menarche (before 12 years of age), late menopause (at age 55 years and later), the first pregnancy terminated by abortion, infertility, age at first birth (30 years and later), breast feeding, reproductive losses, proliferative changes in breast tissues, BrCa in health history of immediate relatives, education, height, body mass index, smoking and some others [2, 5–23].

Breast is well known to be among the most radiosensitive organs [24, 25]. A review issued

Anna V. Rumyantseva – Candidate of Biological Sciences, researcher (e-mail: clinic@subi.su; tel.: +7 (35130) 2-95-84; ORCID: https://orcid.org/0000-0002-3056-3395).

Tamara V. Azizova – Candidate of Medical Sciences, Deputy Director for Science, Head of Clinical Department (e-mail: clinic@subi.su; tel.: +7 (35130) 2-95-84; ORCID: https://orcid.org/0000-0001-6954-2674).

Maria V. Bannikova – Junior researcher (e-mail: clinic@subi.su; tel.: +7 (35130) 2-95-84; ORCID: https://orcid.org/0000-0002-2755-6282).

by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) revealed that ionizing radiation (IR) was associated to elevated risks of BrCa [26].

Preston and colleagues [27] analyzed mortality due to BrCa in a combined cohort that included atomic bomb survivors of Hiroshima and Nagasaki (Life Span Study, LSS, Japan) and seven other cohorts comprised of individuals who had undergone radiotherapy for benign neoplasms, communicable diseases and endocrine pathologies. The analysis revealed a linear association of mortality due to BrCa with a radiation dose [28]. Meanwhile, available data on dose-response relationship for BrCa incidence following chronic radiation exposure at low doses are sparse [24, 29]. There are practically no data on effects of known non-radiation factors on incidence of BrCa in cohorts of individuals exposed to IR.

Our research aim was to assess a relative risk (*RR*) of BrCa incidence among females who were occupationally exposed to chronic IR taking into account radiation and non-radiation factors.

Materials and methods. This is a retrospective cohort study. The considered cohort included all females (the total of 5,689) who were employed at the first nuclear enterprise in the former USSR, the Mayak Production Association (PA), in 1948–1982. The cohort members were identified based on occupational histories provided by "The Mayak worker dosimetry system – 2013" (MWDS–2013) [30]. A percentage of workers who were hired at the enterprise prior to 1954 was 51.34 %. The majority of females (95 %) started working at the Mayak PA at their reproductive age (18–45); the average age at the start of employment was 27.32 (standard deviation (*SD*) 7.97) years. As of December 31, 2018, information was available for 95.8 % of females; 3,346 (58.8 %) of them had died (the average attained age was 72.07 years) and 2,103 (37.0 %) were alive (the average age was 75.82 years). The follow-up of the cohort started at the date of hire at one of the main Mayak PA facilities and was ongoing until one of the following dates: date when BrCa was diagnosed; date of death; December 31, 2018 for females who were known to be alive and living in Ozyorsk; date of the last medical record for females who left Ozyorsk for another place of permanent residency (migrants).

Based on data provided by the "Clinic" medical-dosimetric database, 157 females with diagnosed BrCa (malignant neoplasm of breast, C50 in ICD-10) were identified.

Gamma-ray doses from external exposure were available for the whole cohort in the MWDS–2013 [30]. The average duration of employment that involved contacts with gamma-ray sources was 15.6 (10.55) years. The mean cumulative breast absorbed gamma-ray dose from external exposure was 0.45 (0.72) Gy.

We should note that MWDS–2013 does not provide dose estimates for internal radiation exposure of breast but it provides muscle absorbed alpha-particle doses from internal exposure caused by incorporated plutonium. Therefore, in our study we used these doses estimated at the moment of BrCa diagnosis. The mean cumulative muscle absorbed alpha-particle dose from internal exposure due to incorporated plutonium was 0.001 (0.002) Gy.

The analysis estimated the BrCa incidence *RRs* in relation to various non-radiation (attained age, reproductive characteristics, concomitant pathology, height, body mass index (BMI), postmenopausal obesity, BrCa in immediate relatives, education, smoking, alcohol intake, a calendar period of BrCa diagnosis, age and period at hire at the Mayak PA) and radiation factors (external gamma-ray and neutron exposure and internal alpha-particle exposure due to incorporated plutonium).

We performed a categorical data analysis and calculated the BrCa incidence *RRs* for categories of cumulative breast absorbed doses of external gamma-ray exposure (< 0.2 Gy, 0.2–0.5 Gy, 0.5–1.0 Gy, ≥ 1.0 Gy); categories of cumulative muscle absorbed doses of internal alpha-particle exposure (< 0.001 Gy, 0.001–0.005 Gy, ≥ 0.005 Gy); and categories of cumulative muscle absorbed doses of neutron exposure (< 0.0001 Gy, 0.0001–0.0005 Gy, ≥ 0.0005 Gy). Reference groups included workers who were exposed to the lowest doses

(< 0.2 Gy for external gamma-ray exposure; < 0.001 Gy for internal alpha-particle exposure; and < 0.0001 Gy for neutron exposure).

The categorical data analysis that estimated the BrCa incidence *RRs* was performed in two ways: without stratification (Model 1) and with stratification by attained age and calendar period (Model 2).

The association of the BrCa incidence *RR* with internal alpha-particle exposure was analyzed for a subcohort of workers monitored for internal exposure. The association of the BrCa incidence *RR* with neutron exposure was analyzed only for workers who had been occupationally exposed to neutrons.

The *RR* analysis was based on the Poisson's regression and run with AMFIT module of the EPICURE software package [31]. Data were grouped into multidimensional arrays using DATAB module of the EPICURE software package. 95 % confidence intervals (CI) were calculated for *RRs* with maximum likelihood estimation. The results were considered statistically significant at $p < 0.05$.

Results. Malignant neoplasms (Chapter II in ICD-10) accounted for 1.9 % in the pattern of chronic morbidity among females of the study cohort and BrCa held the first place among them (17.6 %).

By December 31, 2018, data were available for all females diagnosed with BrCa: 21 % were alive and 79 % had died. The average age of those who were alive was 80.61 (6.17) years (the median age was 80 years; the minimum age was 67 years, the maximum age was 90 years); the average age of those who had died was 70.96 (12.35) years (the median age was 73.5 years; the minimum age was 28 years; the maximum age was 92 years).

Over the whole follow-up period, 157 females with verified BrCa were identified in the cohort. The average age of BrCa diagnosis was 62.89 (13.10) years (the median age was 65 years; the minimum age was 28 years; the maximum age was 90 years). 8 females had bilateral metachronous BrCa, i.e. BrCa was diagnosed in another breast 6 months later after the first BrCa diagnosis. Therefore, the number of cases identified in 157 females was 165; among them 82 cases (49.7 %) were tumor of a left breast and 83 cases (50.3 %) were tumors of a right breast. 13 females (8.3 %) also had another malignant neoplasm diagnosed prior to BrCa.

Table 1 provides data on BrCa incidence *RRs* in the analyzed cohort by attained age of females.

The *RRs* of BrCa incidence were statistically significantly lower than 1 in all age groups compared to a group of females over 70 year of age (the reference group). The BrCa incidence *RR* increased with increasing attained age.

Table 2 summarizes data on BrCa incidence *RRs* in the analyzed cohort by reproductive characteristics.

The analysis revealed that the BrCa incidence *RR* was elevated in females with age at menarche of 13 years and above and increased with increasing age at menarche; however, the statistically significant *RR* was detected only in females with age at menarche of 18 years and above (Model 1). However, once adjustments for age and calendar period were included in the model, the risk became statistically non-significant.

Table 1

Relative risk of BrCa incidence by attained age

Attained age, years	Number of cases	Person-years of the follow-up / 100,000	Relative risk (95 % confidence interval) (Model 1)	Relative risk (95 % confidence interval) (Model 2)
< 40	9	0.54912	0.07 (0.03, 0.14)	0.13 (0.05, 0.33)
40–49	21	0.36711	0.25 (0.15, 0.40)	0.34 (0.17, 0.65)
50–59	31	0.34663	0.39 (0.25, 0.59)	0.48 (0.28, 0.82)
60–69	39	0.28093	0.60 (0.40, 0.90)	0.68 (0.43, 1.06)
> 70	57	0.24585	1	1

Table 2

Relative risk of BrCa incidence by reproductive characteristics

Characteristic	Number of cases	Person-years of the follow-up / 100,000	Relative risk (95 % confidence interval) (Model 1)	Relative risk (95 % confidence interval) (Model 2)
Age of menarche, years				
< 13	18	0.26422	1	1
14–15	59	0.74931	1.16 (0.70, 2.02)	0.93 (0.56, 1.64)
16–17	42	0.46862	1.32 (0.77, 2.34)	1.09 (0.63, 1.98)
> 18	23	0.17073	1.98 (1.07, 3.71)	1.62 (0.86, 3.11)
Age of menopause, years				
< 44	19	0.1418	1.48 (0.87, 2.41)	1.74 (1.02, 2.82)
45–49	39	0.48423	0.89 (0.60, 1.31)	0.95 (0.64, 1.39)
50–54	71	0.78586	1	1
> 55	9	0.12096	0.82 (0.38, 1.56)	0.82 (0.38, 1.56)
Female infertility (Chapter XIV of ICD-10, N97)				
no	154	1.66065	1	1
yes	3	0.08642	0.37 (0.09, 0.99)	0.34 (0.09, 0.91)
Age at live birth, years				
< 24	88	1.01416	1	1
25–29	45	0.44132	1.18 (0.81, 1.67)	1.14 (0.78, 1.64)
> 30	11	0.12317	1.03 (0.52, 1.84)	1.18 (0.58, 0.21)
The first pregnancy terminated by abortion				
no	135	1.53303	1	1
yes	16	0.20354	0.89 (0.51, 1.45)	0.89 (0.51, 1.45)
Number of births				
1	26	0.34499	1	1
2	90	0.92107	1.30 (0.85, 2.05)	1.11 (0.73, 1.76)
3	25	0.27666	1.20 (0.69, 2.08)	1.01 (0.58, 1.76)
> 4	8	0.12123	0.88 (0.37, 1.85)	0.83 (0.35, 1.79)
Number of abortion				
0	19	0.34073	1	1
1–2	49	0.49395	1.78 (1.07, 3.10)	1.55 (0.92, 2.70)
3–5	54	0.55259	1.75 (1.06, 3.03)	1.37 (0.82, 2.38)
> 6	32	0.37803	1.52 (0.87, 2.73)	1.08 (0.61, 1.97)

We detected the statistically significant elevated *RR* of BrCa incidence for females who had menopause at age below 45.

The BrCa incidence *RR* was statistically significantly lower among females with diagnosed infertility in comparison with those without infertility. However, one should be very careful when interpreting this result since only 3 females (1.91 %) with diagnosed infertility were identified in the analyzed cohort.

We detected the elevated, though statistically non-significant, BrCa incidence *RR* for females who had given birth to the first child at age above 25 years. The BrCa incidence *RR* was below 1 in females who had terminated their first pregnancy by abortion compared to females who had taken pregnancies to terms but the detected risk was statistically non-significant.

The analysis of BrCa incidence in relation to a number of births revealed the elevated (though statistically non-significant) *RR* in females with 2 or 3 births in health histories compared to those with only one birth. Moreover, the BrCa incidence *RR* was lower (though statistically non-significantly) in females with 4 or more births.

Females who had several abortions demonstrated the elevated BrCa incidence *RR* (significant when estimated with Model 1) compared to females without reproductive losses.

Table 3 summarizes data on BrCa incidence *RRs* in the analyzed cohort in relation to a concomitant pathology.

The analysis revealed the statistically significant elevated *RR* of BrCa incidence in females with benign mammary dysplasia, benign neoplasms of breast and leiomyoma of uterus (Table 3).

The analyses based on Model 1 found statistically significant elevated risks of BrCa in females with diabetes mellitus, hypertensive diseases, and neurotic, stress-related and somatoform disorders. When the risk analysis was run using Model 2, the corresponding *RR* estimates levelled down considerably and the risk became statistically non-significant.

Table 4 summarizes *RRs* of BrCa incidence in the analyzed cohort in relation to non-radiation factors.

The analysis revealed the statistically significant elevated *RR* of BrCa incidence in females who were higher than 170 cm compared to those whose height was 150–170 cm. In addition, the elevated (though statistically non-significant) risk of BrCa incidence was detected in females with BMI > 25 kg/m^2 and with post-menopausal obesity ($p < 0.05$ with Model 1).

The BrCa incidence *RR* was elevated ($p > 0.05$) in females whose immediate relatives were diagnosed with BrCa.

The reduced *RR* of BrCa incidence ($p < 0.05$) was detected in females with higher education compared to those without higher education (based on Model 1).

The BrCa incidence *RR* was elevated, though statistically non-significant, in females who had ever smoked. The BrCa incidence *RR* was reduced among alcohol abusers but there were only 2 females in this category with alcohol drinking habit and this result should be interpreted very carefully (due to the insufficient statistical power).

Table 5 provides BrCa incidence *RRs* in the analyzed cohort in relation to a calendar period of BrCa diagnosis and non-radiation occupational factors.

The analysis based on Model 1 revealed BrCa incidence *RRs* below 1 ($p < 0.05$) in all categories of calendar period of BrCa diagnosis (except for 2006–2008) compared to 1991–2005 period. No statistically significant association was observed for BrCa incidence with a period of hire at the Mayak PA. Meanwhile, the elevated *RR* of BrCa incidence was detected in females hired at the Mayak PA at age above 30 years compare to those hired at age between 20 and 30 years.

Table 3

Relative risk of BrCa incidence in relation to a concomitant pathology

Factor	Number of cases	Person-years of the follow-up / 100,000	Relative risk (95 % confidence interval) (Model 1)	Relative risk (95 % confidence interval) (Model 2)
Benign mammary dysplasia (N60 in ICD-10)				
no	140	1.71181	1	1
yes	17	0.03468	5.99 (3.49, 9.62)	3.90 (2.24, 6.36)
Benign neoplasms of breast (D24 in ICD-10)				
no	140	1.71459	1	1
yes	17	0.0319	6.53 (3.80, 10.48)	4.64 (2.70, 7.48)
Leiomyoma of uterus (D25 in ICD-10)				
no	118	1.452	1	1
yes	39	0.29564	1.62 (1.12, 2.31)	0.96 (0.65, 1.38)
Type 1 and 2 diabetes mellitus (E10–E11 in ICD-10)				
no	144	1.7168	1	1
yes	13	0.07285	2.13 (1.15, 3.60)	1.00 (0.53, 1.71)
Hypertensive diseases (I10–I15 in ICD-10)				
no	67	1.26266	1	1
yes	90	0.52698	3.22 (2.35, 4.43)	1.29 (0.88, 1.91)
Neurotic, stress-related and somatoform disorders (F40–F48 in ICD-10)				
no	52	0.84505	1	1
yes	105	0.9446	1.81 (1.30, 2.54)	1.02 (0.73, 1.44)

Table 4

Relative risks of BrCa incidence in relation to non-radiation factors

Factor	Number of cases	Person-years of the follow-up / 100,000	Relative risk (95 % confidence interval) (Model 1)	Relative risk (95 % confidence interval) (Model 2)
Height, cm				
< 150	5	0.09305	0.64 (0.23, 1.40)	0.65 (0.23, 1.43)
150–170	130	1.54558	1	1
> 170	9	0.05153	2.08 (0.98, 3.85)	2.64 (1.24, 4.91)
BMI (kg/m^2)				
< 18.5	14	0.25033	0.53 (0.28, 0.96)	0.57 (0.3, 1.03)
18.5–24.9	39	0.3723	1	1
≥ 25	46	0.34947	1.26 (0.82, 1.93)	1.25 (0.82, 1.93)
Postmenopausal obesity (E66 in ICD-10)				
no	119	1.5677	1	1
yes	38	0.22194	2.26 (1.55, 3.22)	0.92 (0.61, 1.36)
BrCa in immediate relatives				
no	104	0.71004	1	1
yes	5	0.02405	1.42 (0.50, 3.14)	1.58 (0.56, 3.5)
Education				
not higher	140	1.50888	1	1
higher	11	0.21895	0.54 (0.28, 0.95)	0.68 (0.35, 1.20)
Smoking				
never smoked	144	1.66776	1	1
has been a smoker	9	0.09867	1.06 (0.5, 1.95)	1.34 (0.63, 2.50)
Alcohol intake				
never drank	85	0.92939	1	1
a moderate drinker	66	0.74429	0.97 (0.70, 1.34)	0.87 (0.62, 1.22)
alcohol abuser	2	0.07328	0.30 (0.05, 0.94)	0.38 (0.06, 1.20)

Table 5

Relative risks of BrCa incidence in relation to a calendar period of BrCa diagnosis and non-radiation occupational factors

Factor	Number of cases	Person-years of the follow-up / 100,000	Relative risk (95 % confidence interval) (Model 1)	Relative risk (95 % confidence interval) (Model 2)
Calendar period of BrCa diagnosis, years				
< 1960	2	0.25467	0.06 (0.01, 0.18)	0.49 (0.07, 2.04)
1961–1975	16	0.40781	0.27 (0.15, 0.46)	0.82 (0.40, 1.64)
1976–1990	38	0.50502	0.52 (0.35, 0.78)	0.90 (0.56, 1.43)
1991–2005	60	0.41812	1	1
2006–2018	41	0.20403	1.4 (0.94, 2.08)	1.12 (0.72, 1.73)
Period of hire at the Mayak PA, years				
1948–1953	67	0.80503	1	1
1954–1958	19	0.23603	0.97 (0.57, 1.58)	0.97 (0.57, 1.58)
1959–1982	71	0.74859	1.14 (0.82, 1.59)	1.14 (0.82, 1.59)
Age at hire, years				
< 20	19	0.32094	0.77 (0.45, 1.24)	0.82 (0.47, 1.36)
20–30	73	0.94314	1	1
> 30	65	0.52556	1.60 (1.14, 2.23)	1.30 (0.91, 1.86)

Table 6

Relative risk of BrCa incidence in relation to cumulative breast absorbed gamma-ray dose of external exposure

	Cumulative dose of external gamma-ray exposure, Gy			
	< 0.2	0.2–0.5	0.5–1.0	> 1.00
Number of cases	91	26	18	22
Person-years of follow-up / 100,000	0.96002	0.2781	0.20983	0.27402
Relative risk (95 % confidence interval) (Model 1)	1	0.99 (0.63, 1.50)	0.91 (0.53, 1.46)	0.85 (0.52, 1.32)
Relative risk (95 % confidence interval) (Model 2)	1	0.89 (0.56, 1.37)	0.88 (0.51, 1.46)	0.81 (0.49, 1.31)

Table 7

Relative risk of of BrCa incidence in relation to cumulative breast absorbed dose of neutron exposure

	Cumulative dose of neutron exposure, Gy			
	0	< 0.0001	0.0001–0.0005	> 0.0005
Number of cases	137	8	6	6
Person-years of the follow-up / 100,000	1.56911	0.04058	0.05842	0.05842
Relative risk (95 % confidence interval) (Model 1)	–	1	0.52 (0.17, 1.50)	1.27 (0.50, 2.63)
Relative risk (95 % confidence interval) (Model 2)	–	1	0.49 (0.16, 1.41)	0.49 (0.16, 1.41)

Table 8

Relative risk of BrCa incidence in relation to cumulative muscle absorbed alpha-particle dose of internal exposure

	Cumulative dose of internal alpha-particle exposure, Gy		
	< 0.001	0.001–0.005	> 0.005
Number of cases	82	15	3
Person-years of the follow-up / 100,000	0.934	0.13898	0.04014
Relative risk (95 % confidence interval) (Model 1)	1	1.23 (0.68, 2.07)	0.85 (0.21, 2.27)
Relative risk (95 % confidence interval) (Model 2)	1	0.75 (0.41, 1.29)	0.57 (0.14, 1.55)

Tables 6–8 summarize *RRs* of BrCa incidence in the analyzed cohort in relation to cumulative doses of occupational radiation exposure.

The analysis did not reveal an association of BrCa incidence with either cumulative breast absorbed gamma-ray dose of external exposure, neutron dose or alpha-particle dose of internal exposure.

Discussion. The results of the study demonstrated that BrCa incidence in the cohort of female nuclear workers employed at the Mayak PA was associated with many non-radiation factors and the results were mostly in line with those obtained in other studies [2, 5, 6, 8, 12, 14–22, 32].

For example, the risk of BrCa incidence increased with increasing attained age what could be expected [2, 5, 6] and was consistent with observations of many other studies.

In contrast to a number of studies reporting that early age at menarche (before 13 years) increased risks of BrCa [8–10], we detected the statistically significant elevated risk of BrCa incidence in females with age at menarche 18 years and older (based on Model 1). With inclusion of additional adjustments for age and calendar period in the model (Model 2), the risk remained elevated but became statistically non-significant. We also detected the elevated risk of BrCa in females of the study cohort who had

menopause at age below 45 years while some other studies [9, 11] revealed that late menopause (at age above 55) increased BrCa risks.

The study demonstrated the elevated risk of BrCa incidence in females with late age at first birth (above 25 years) and this agreed well with results observed in some other studies [6, 9, 10, 13].

The BrCa incidence *RR* was lower in those females of the analyzed cohort who had four or more births ($p < 0.05$) and this was consistent with the results of a meta-analysis [14] and a number of other studies [8] that demonstrated decreased risks of BrCa with increasing number of pregnancies and births.

We revealed the elevated risk of BrCa incidence in females of the study cohort who terminated their pregnancies by abortion and this agreed with other research results reporting that three or more abortions led to a considerable increase in risks of BrCa [15, 16].

This study demonstrated the elevated risk of BrCa incidence in females with fibrocystic breast disease and benign neoplasms of breast registered prior to BrCa in health histories and this agreed well with results of other studies [6, 17, 18].

We revealed the statistically significant elevated risk of BrCa incidence in females of the study cohort who had a concomitant pathology (leiomyoma of uterus, diabetes mellitus, hypertensive diseases, or neurotic disorders) prior to BrCa and this was consistent with results of other studies [5, 15, 16, 18–20]. Meanwhile, we should note that the risks became non-significant when we used the model that included additional adjustments for attained age and calendar period (Model 2). This result was most likely observed due to insufficient statistical power of the additional analyses but this needs further investigation.

The present analysis revealed a relationship between incidence of BrCa and height and BMI and this agreed with results of other studies [5, 15, 16]. Thus, the follow-up of females aged 30–69 years (approximately 570,000) during 6–18 years revealed that tall women in all age groups were at high risks of BrCa [21]. Overweight is another risk factor of BrCa since the imbalance of extra-ovarian estrogens produced in fat tissues during the reproductive period results in elevated risks of BrCa [26]. According to a number of studies, the present one included, postmenopausal obesity is an established factor that increases the risk of BrCa [5, 6, 8, 12, 15, 18, 22].

The present study revealed elevated risks of BrCa for females having immediate relatives with BrCa and this agreed well with other studies that provided evidence to 6–7 times higher risks of BrCa in females whose genetic relatives had BrCa [5, 6].

A number of studies have revealed a positive statistically significant correlation between alcohol intake (even moderate) and risks of BrCa incidence [6]. However, similar to an earlier study [32], we did not find any evidence that could prove this; it was probably due to the insufficient statistical power of the analysis with only two females assigned to the category of 'alcohol abuse' in the analyzed cohort. In contrast, the analysis revealed the elevated risks of BrCa incidence associated with smoking and this agreed well with results of other studies demonstrating the BrCa incidence *RR* of 2.3 for smoking females even with many other factors taken into account [16].

BrCa incidence in females of the study cohort was not associated with cumulative breast absorbed gamma-ray dose of external exposure, cumulative muscle absorbed alpha-particle dose of internal exposure, or cumulative breast absorbed neutron dose.

Conclusion. The results of the presented cohort study that considered female nuclear workers who had been chronically exposed to IR suggested that BrCa incidence was associated with many non-radiation factors (attained age, age at menarche, age at menopause, number of abortions, concomitant diseases prior to BrCa (fibrocystic breast disease, benign neoplasms of breast, leiomyoma of uterus, diabetes mellitus, hypertensive diseases, stress and neurotic disorders, postmenopausal obesity), height, BMI, age at hire at the Mayak PA) and was not associated with occupational radiation exposure. Meanwhile,

we revealed the risk estimate close to 1 with the upper limit of the confidence interval being higher than 1 by 30–50 %. Since the statistical power of the performed analyses was not high, the observed findings should not be considered as conclusive. The follow-up of the cohort of Mayak PA female workers is ongoing and in future an excess relative risk of BrCa incidence per unit breast absorbed radiation dose and a lifetime risk of BrCa incidence will be estimated considering the extended follow-up period and the updated information on members of the cohort.

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