without familial history, according to age at diagnosis and year of treatment. The follow-up of controls was at least equal to the time-interval between diagnosis and genetic testing in cases. The 136 tumors were matched to 271 controls. Rates of BR as first event and CBC as any event were determined using Kaplan-Meier estimates, and comparisons done with the log-rank test. A multivariate analysis using a Cox's stepwise forward regression model was done to determine the independent prognostic value of various factors on breast recurrence.

Results: *BRCA1/2* mutations were found in 20.6% pts. with a family history (21.3% tumors). Nineteen pts. (with 21 tumors) had a *BRCA1* mutation, and 8 had a *BRCA2* mutation. Breast cancers in mutation carriers were more often of grade III ($p<10^{-4}$) and estrogen receptor negative (p=0.005) than tumors in both non-carriers and controls. Medullary subtype was more frequent in *BRCA1* carriers than in other groups (11.5% vs 1.2% vs 0.9%, respectively). Median follow-up for all 392 pts. was 8.75 years (2.25–19.4 yrs.). No significant differences in BR as first event were seen between *BRCA1/2* tumors and controls (p=0.46), tumors in *BRCA1/2* carriers and non-carriers with a family history (p=0.96), or non-carriers and controls (p=0.10). On multivariate analysis, age was the only factor significantly predicting for BR, with an increased relative risk of 6% for every decreasing year of age. The rate of CBC was significantly increased in all pts. with a family history: *BRCA1/2* carriers vs. controls (p=0.0003), non-carriers vs. controls (p=0.0034), and carriers vs. non-carriers (p=0.02).

Conclusion: With a median 9-year follow-up after BCT, the rate of breast recurrence was not higher in *BRCA1/2* mutation carriers than in non-carriers, or than in patients without family history, despite more aggressive tumor features and a higher risk of CBC. Tumors in *BRCA* carriers may be more sensitive to radiation, possibly through an impaired DNA double-strand break repair capacity. Therefore, BRCA mutation carriers can be offered breast-conserving treatments of breast cancer. However, further follow-up will need to ensure that the rate of new breast cancer in the treated breast does not increase.

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Contralateral breast cancer and survival in non-BRCA1/2 hereditary breast cancer: a case control study

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Background: Most hereditary breast cancers (HBC) cannot be attributed to a germ-line mutation in BRCA1 or BRCA2. Specific histopathologic characteristics have been described in these non-BRCA1/2 hereditary cancers, such as more frequent low grade tumours, low mitotic count, a lower proliferation rate and more lobular carcinoma, discriminating them from both sporadic and BRCA1/2 breast cancers [1–3]. Few data exist on factors influencing survival of proven non-BRCA1–2 breast cancers, although a higher frequency of contralateral cancers as compared to sporadic cancers has been reported [4].

Therefore we assessed the incidence of second breast cancers and disease free and overall survival in patients with hereditary breast cancer but no BRCA1/2 gene mutation. We'll try to assess the impact of prognostic and treatment factors.

Methods: We selected all 236 women registered in the Erasmus University Medical Centre with primary breast cancer diagnosed between 1–1-1980 and 31–12–2002 and a family history of at least 3 confirmed breast or breast and ovarian cancers, but a negative test for a BRCA1 or BRCA2 mutation. Patients with unknown tumour stage or <6 months follow-up were excluded. To each case a control patient without a family history was matched for age at onset and year of diagnosis. Tumour and treatment characteristics were extracted from medical files. Kaplan-Meier curves were used to estimate the occurrence of ipsilateral and contralateral breast cancer, local and distant disease free survival (DFS) and overall survival (OS).

Results: In the 236 cases;mean age at diagnosis was 45 years (range 23–77); the median follow-up 6.1 years (0.56–21.8). Tumours were preinvasive in 5% and <2 cm in 63%; 52% was node-negative. The histologic grade of the tumours was I in 7%, II in 20%, III in 41%, unknown in 32%. Breast conserving therapy (BCT) was performed in 49%, mastectomy in 47%. 37% received adjuvant chemotherapy. Contralateral preventive mastectomy was performed in 10%, risk reducing oophorectomy in 6.7%. On average, the yearly incidence of metachronous second breast cancer was 1.8%. The 5, 10 and 15-year contralateral breast cancer incidence for women with their first BC detected <50 year was 12%, 16% and 25% respectively and 6%, 8% and 8% for women over this age. Distant DFS at 5, 10 and 15-year was 75%, 62% and 56% respectively; OS 86%, 71% and 61%.

Conclusion: Especially in patients diagnosed under age 50 years, contralateral breast cancer incidence appeared to be much higher than expected for sporadic patients, but lower than the rate that was found in our BRCA1 patients. Contralateral BC incidence had no impact on survival. Analyses including the matched controls and the impact of different therapies on survival will be presented. These results are important for the counselling of hereditary breast cancer patients without a BRCA 1/2 germline mutation.

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High prevalence of BRCA1 mutations in breast + ovarian cancer patients at the region of Gdansk, Poland

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Background: Coexistence of breast and ovarian cancer constitutes a significant predictive factor for *BRCA1* positivity.

Material and methods: Prevalence of BRCA1 mutations was analyzed in breast–ovarian cancer syndrome patients registered at the Regional Cancer Registry of Gdansk region, Poland. The screening covered the most common founder mutations. Methods included ASA PCR (exon 2 and 20) and RFLP PCR (exon 5). Prescreening for 3819del5 in exon 11 was performed with nondenaturating polyacrylamide electrophoresis.

Results: Sixty-three cases of coexisting breast and ovarian cancers were found among 9436 breast cancer cases and 2388 ovarian cancer cases registered. The age at diagnosis of breast cancer was 30 to 81 years (median 50 years) and at the diagnosis of ovarian cancer – 30 to 79 years (median 52 years). Seven patients had their first cancer (breast – 4 cases, ovarian – 2 cases, both – 1 case) diagnosed before the age of 40. There were 5 cases of synchronous cancers. The time span between metachronous malignancies varied between 4 and 287 months (median 49 months). Breast cancer preceded ovarian cancer in 46 patients and followed in 12.

Five patients had bilateral breast cancer, the second tumor occurred after a median of 63 months (range 37–134 months). Family history of breast and/or ovarian cancer was positive in 19 of 42 patients with available data. In 10 patients multiple family members were affected. In 42 patients no readily identifiable risk factors for the breast-ovarian cancer syndrome were present. In 2 patients third primary cancer was diagnosed (vulva, thyroid). One patient developed 2 subsequent primary malignancies (endometrium, skin).

BRCA1 typing was performed in 22 patients and mutations were found in 10. Three types of mutations included well known global and European founder mutations were found: 5382insC (6 cases), 185delAC (2 cases) and 300T>G (1 case). The less frequent 3819del5 mutation (1 patient) was recently found in the Polish population.

All patients with germline mutations had a strong family history of breast and/or ovarian cancer (at least 2 cases in all but one patient). In two patients breast cancer occurred before the age of 40, whereas all ovarian cancers occurred after that age. One patient had bilateral breast cancer.

Conclusion: High prevalence of founder BRCA1 mutations was found among breast-ovarian cancer syndrome patients from the region of Gdansk, Poland. Strong family history was the best predictor of BRCA1 positivity in this population.