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Metachrone contralateral breast cancers: Differences in detection mode, Nottingham Prognostic Index, ER, PR and HER2

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BACKGROUND and AIM

- The risk of contralateral breast cancer within 25 years after the initial diagnosis is 9,9%, with an annual cumulative risk of 0,37%[1]
- Risk factors for contralateral breast cancer have been extensively studied in previous research[2,3]
- Little is known about the tumor characteristics of metachronous contralateral breast cancers in real-world datasets.

The aim was to investigate how metachronous contralateral breast cancers are detected, what their tumor characteristics are, and whether receptor profiles resemble those of the initial tumor, based on real-world clinical data.

PATIENTS and METHODS

Study population

A single-center retrospective analysis at UZ Leuven was performed of women diagnosed with an invasive contralateral breast cancer (CBC) > 3 months after the first invasive breast cancer in the other breast was detected between 2000 and 2023. The following inclusion criteria were applied:

- Female patients with histologically confirmed metachronous CBC
- Availability of complete pathology reports for both lesions

For each patient, the following tumor characteristics were collected for both lesions:

- Detection mode
- Histological subtype (ILC vs non-ILC)
- NPI
- Receptor type: ER, PR (PR ≥1% = positive), and HER2 status (amplified = positive)

We also evaluated patient-related variables which could influence changes in tumor type between lesion 1 and lesion 2.

Statistical analyses

Continuous variables were analyzed using the Mann-Whitney U test; categorical variables with the Chi² test. Paired comparisons used the Wilcoxon signed-rank test. Predictors of histologic change were assessed via logistic regression. Analyses were performed in SAS (v9.4), with $p < 0.05$ considered significant

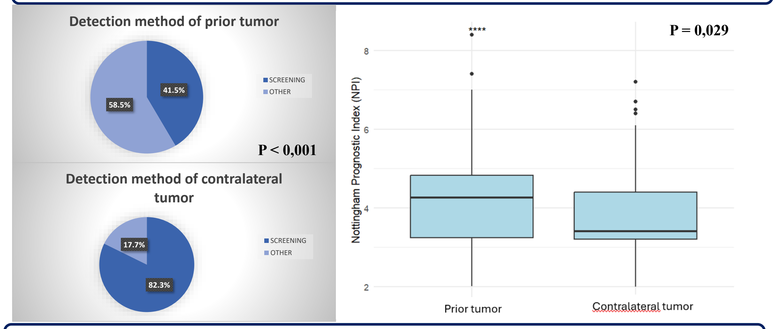
RESULTS

Demographics

3.39% of patients with a first breast cancer developed a contralateral tumor. We included 289 patients in this study.

	Average	Standard deviation (SD)	Total measured (N)
Age	54,9 y	10,5 y	289
BMI	25,8 kg/m²	5 kg/m²	272
Age at menarche	13,3 y	1,6 y	235
First full-term pregnancy	26,2 y	5,1 y	174
Delay between first and second lesion	8,9 y	5,2 y	289

Differences in detection method and NPI



Association in hormone receptor status

Estrogen receptor (ER)

Variable	Statistic	ER negative	ER positive	P-value
type_T2				
ER negative	n/N (%)	22/68 (32.35%)	32/221 (14.48%)	**<0.001**
ER positive	n/N (%)	46/68 (67.65%)	189/221 (85.52%)	

Table: Columns refer to Estrogen receptor-status in tumor 1; rows refer to ER-status in tumor 2 . All reported P-values are two-sided

The ER-status of the contralateral tumor was significantly predicted by the ER-status of the 1st lesion.

Change in ER-status was affected by later age at menarche (OR 1.239; 95% CI 1.030; 1.490).

Progesterone receptor (PR)

Variable	Statistic	PR negative	PR positive	P-value
type_T2				
PR negative	n/N (%)	38/88 (43.18%)	61/201 (30.35%)	**0.034**
PR positive	n/N (%)	50/88 (56.82%)	140/201 (69.65%)	

Table: Columns refer to Progesterone receptor-status in tumor 1; rows refer to PR-status in tumor 2 . All reported P-values are two-sided

The PR-status of the contralateral tumor was significantly predicted by the PR status of the 1st lesion.

None of the tested variables affected changes in PR-status.

Comparing HER2 status and histological subtype

HER2 status

Variable	Statistic	HER2 negative	HER2 positive	P-value
type_T2				
HER2 negative	n/N (%)	216/243 (88.89%)	29/35 (82.86%)	0.302
HER2 positive	n/N (%)	27/243 (11.11%)	6/35 (17.14%)	

Table: Columns refer to Human Epidermal growth factor Receptor 2-status in tumor 1; rows refer to HER2-status in tumor 2 . All reported P-values are two-sided

The change in HER-2 status was not significant.

None of the tested variables affected changes in HER2-status.

Histological subtype

Variable	Statistic	Non-ILC	ILC	P-value
type_T2				
non-ILC	n/N (%)	213/249 (85.54%)	28/40 (70.00%)	**0.014**
ILC	n/N (%)	36/249 (14.46%)	12/40 (30.00%)	

Table: Columns refer to histologic subtype non-ILC/ILC in tumor 1; rows refer to non-ILC/ILC in tumor 2 . All reported P-values are two-sided

The histologic subtype of lesion 2 was predicted by that of lesion 1.

None of the tested variables affected changes in histological subtype.

CONCLUSIONS

Contralateral breast tumors may develop > 10 years after the initial diagnosis, regardless of initial hormonal receptor status.

These tumors are more often **screen-detected** and associated with a more favorable **NPI**.

Histological subtype and receptor status frequently change between lesions.

Lobular histology and **hormonal receptor** status were stronger **predictors** of contralateral tumor characteristics than HER2-status.

ABBREVIATIONS

- ER = Estrogen Receptor
- PR = Progesterone Receptor
- HER2 = Human Epidermal growth factor Receptor 2
- CBC = Contralateral Breast Cancer
- ILC = Invasive Lobular Carcinoma
- NPI = Nottingham Prognostic Index
- SD = Standard Deviation
- N = Total measured
- BMI = Body Mass Index
- OR = Odds Ratio
- CI = Confidence Interval

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