

Predicting breast cancer risk in childhood cancer survivors treated with chest radiation: A Report from the Childhood Cancer Survivor Study (CCSS), and the Dutch Hodgkin Late Effects and DCOG-LATER Cohorts.

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Background: Chest radiotherapy (RT) increases breast cancer (BC) risk in childhood cancer survivors. Absolute risk BC prediction models applicable to this population are not available.

Methods: Among 1,150 female 5-year survivors diagnosed < 21 years old and treated with chest RT in CCSS (median age at last follow-up 43 years, median follow-up 32 years), 241 were diagnosed with invasive or *in situ* breast cancer. Using these data we combined BC relative risks with the competing risk of death to predict the absolute risk of BC based on treatment exposures and BC risk factors. Variables maximizing the competing risk time-dependent area under the curve (AUC) were selected. Data from two Dutch cohorts on 470 female 5-year survivors of cancer diagnosed < 21 years old (median age at last follow-up 38 years, median follow-up 29 years, 84 with BC) were combined for validation.

Results: The final BC model included: chest RT field, receipt of chest RT within one year of menarche, exposure to anthracyclines, history of a first-degree relative with BC, and age at menopause. The estimated 10-year BC risk varied considerably based on these variables, from 2% to 41% (table), with highest risks among premenopausal women treated with mantle field RT within a year of menarche who had a first-degree relative with BC. In comparison, a typical 40-year old woman without a history of childhood cancer but with a first-degree relative with BC has a 10-year risk of 2.6% (<https://tools.bcsc-scc.org/bc5yearrisk/calculator.htm>). The average AUC on the validation cohort was 0.61.

Conclusions: BC risk varies widely among childhood cancer survivors treated with chest RT. Accurate risk prediction may aid in refining surveillance, counseling, and preventive strategies in this population.

Selected Examples: 10-Year Risk of BC

Current Age, years	Chest RT Field	Chest RT within 1 Year of Menarche	Treated with Anthracyclines	First-degree Relative with BC	Age at Menopause	10-Year Risk
30	Mediastinal	No	Yes	No	Before age 25	2%
30	Whole lung	No	Yes	Yes	Still menstruating	17%
40	Mediastinal	Yes	Yes	Yes	Still menstruating	22%
40	Mantle	Yes	No	Yes	Still menstruating	41%