

**NEW PRIMARY SARCOMAS IN SURVIVORS OF CHILDHOOD CANCER:
A DETAILED ANALYSIS OF THE EFFECTS OF TREATMENT.
A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY.**

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Background: Childhood cancer survivors are at increased risk for the development of subsequent primary sarcomas. Exposure to radiation therapy is a known risk factor for the development of these sarcomas. However, the details of the dose-response relationships, the expression of excess risk over time, and the modifying effects of other host and treatment factors have not been well defined.

Methods: Subsequent sarcomas occurring within a cohort of 14,372 5-year survivors of childhood cancers were ascertained. Each patient was matched with four control subjects by age, sex, and time since original cancer diagnosis. Radiation doses at the site of the subsequent sarcoma were estimated, and chemotherapy information was abstracted from detailed medical records. Conditional logistic regression was used to estimate odds ratios (ORs) and calculate 95% confidence intervals (CIs).

Results: Subsequent sarcomas were identified in 128 individuals. Sarcomas occurred a median of 12.8 years (range = 5.3 - 32.5 years) from original diagnosis. Radiation exposure was associated with increased risk of subsequent sarcomas (OR = 4.4, 95% CI = 2.1 - 9.4). Increased risk was apparent at doses below 10 Gy (OR = 13.0, 95% CI = 4.8 - 35.0) and reached 36-fold for doses above 40 Gy (95% CI = 11.5 - 112.9). Controlling for radiation, prior exposure to anthracyclines (OR = 2.4, 95% CI = 1.1 - 5.2) and bleomycin (OR= 6.4, 95% CI 1.7 - 25.0) were associated with an increased risk of new sarcoma. Alkylator exposure was not significantly associated with risk for sarcoma (OR = 1.5, 95% CI = 0.7 - 3.1).

Conclusions: Exposure to radiation therapy, even at low doses, is the most important risk factor for the development of new sarcomas in childhood cancer survivors. Exposure to certain chemotherapy agents is also associated with risk for subsequent sarcomas.