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.