

1 **2023 Pediatric SNO, ASCO, ISLCCC Conference: Abstract Submission**

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7 **Title:** Subsequent CNS Malignancy Among Survivors of Childhood Cancer: a Report from the  
8 Childhood Cancer Survivor Study (CCSS)

9  
10 **Abstract**

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12 Subsequent malignant neoplasms (SMNs) of the central nervous system (CNS) following  
13 childhood cancer are a frequently fatal late effect of cancer therapy. We used the CCSS (5-year  
14 childhood cancer survivors, diagnosed 1970-1999) to assess whether temporal changes in  
15 therapy have reduced CNS SMN risk. Twenty-year cumulative incidence rates (95% confidence  
16 interval) were estimated, and standardized incidence ratios (SIR, 95% CI) were calculated  
17 comparing observed to expected rates from SEER. Multivariable models assessed demographic  
18 and treatment-related risk factors for CNS SMN. Among survivors diagnosed between 1970-  
19 1979 (N=6223), 1980-1989 (N=9680), and 1990-1999 (N=8999) with median follow-up of 40.5,  
20 32.2, and 22.6 years, respectively, 157 CNS SMNs (1970s, 52; 1980s, 63; 1990s, 42) were  
21 identified, excluding meningiomas. Malignant gliomas (N=131) were the most common SMNs.  
22 Cranial radiotherapy (CRT) exposure decreased by treatment decade, with the proportion of  
23 survivors receiving no CRT increasing from 23.0% (1970s), to 45.7% (1980s), and 66% (1990s).  
24 Decreases in >0-10Gy exposure (39.0% to 14.1%) and 20.1-30Gy (19.2% to 2.4%) were  
25 observed while those receiving >30Gy CRT has not substantially changed (12%, 11.1%, and  
26 8.8%, respectively). Twenty-year cumulative incidence and SIR for development of SMN were  
27 0.32% (0.18-0.46%) and 6.6 (5.0-8.7); 0.55% (0.41-0.70%) and 8.3 (6.6-10.4); and 0.43% (0.31-  
28 0.55%) and 9.2 (7.0-12.0), respectively, with no statistically significant differences between  
29 treatment eras, including when stratified by attained age. Multivariate analysis showed increased  
30 risk for all CRT dose levels >10Gy and for primary diagnoses of medulloblastoma/PNET (HR  
31 3.6, 2.0-6.6) and astrocytoma (HR 2.4, 1.4-3.9). Three-year cumulative incidences of death after  
32 SMN, by treatment decade, were 70%, 73%, and 69%, respectively. In conclusion, CNS SMN  
33 incidence has not decreased despite fewer survivors being treated with CRT, and CNS SMNs  
34 remain a significant source of mortality for affected patients.