

Subsequent Neoplasms (SNs) of the Central Nervous System (CNS) in Survivors of Childhood Cancer: A Case/Control Study from the Childhood Cancer Survivor Study (CCSS). *J. Neglia, P. Inskip, Y Liu, Y. Yasui, S. Hammond, M. Stovall, R. Packer, A Meadows, A. Mertens, L. Robison, CCSS, University of Minnesota, Minneapolis, MN.*

The CCSS is a multi-institutional cohort study of long-term survivors of childhood cancer. We conducted a nested case-control study of therapy and non-therapy related risk factors for CNS SNs among 70 cases and 280 age-, sex-, and survival duration-matched controls. Cases included 35 individuals with secondary meningioma, 28 cases with secondary glial tumors, 4 of secondary PNET, and three with unspecified or other histology. Medical records of cases and controls were abstracted for information on therapy of the original cancer and location of the CNS SN (cases). Site-specific radiation dosimetry was performed to determine dose to the affected area in individual cases and their matched controls. The majority of CNS SNs occurred among survivors of childhood leukemia (n=38) and primary CNS tumors (n=21). Cases were predominately under age 5 at time of original diagnosis (n=37). Radiation therapy prior to the diagnosis of the SN was confirmed among 66 (94%) of the cases and 194 (69%) of the controls. There was no clear association between CNS SNs and chemotherapy exposure of any kind (Odds Ratio (OR) 1.0), or for exposure to specific chemotherapy agents, including alkylating agents (OR=1.1), anthracyclines (OR=0.5), epipodophyllotoxins (OR=1.2), platinum compounds (OR=1.7), or antimetabolites (OR=0.9) [p>0.05 in all analyses, adjusted for radiation exposure]. Sub-group analysis separating cases with meningiomas and glial tumors did not identify additional chemotherapy associations. There was a positive association between radiation dose and risk of both types of CNS SNs, particularly for meningioma, as shown below.

Site-Specific Radiation Dose (cGy)	Odds Ratio (95% Confidence Intervals)					
	Any CNS SN		Secondary Meningioma		Secondary Glial Neoplasm	
0 - 99	1.0	(ref)	1.0	(ref)	1.0	(ref)
100 - 999	0.0	(0.0, undef)	0.0	(0.0, undef)	0.0	(0.0, undef)
1000 - 1999	11.5	(2.9, 45.0)	0.0	(0.0, undef)	17.1	(3.03, 96.2)
2000 - 2999	19.4	(6.2, 61.0)	21.4	(3.2, 141.3)	14.0	(2.9, 67.4)
3000 - 4499	54.6	(11.4, 262.7)	177.9	(11.3, 2806.4)	50.7	(3.2, 812.7)
4500+	47.2	(12.5, 178.1)	63.5	(8.5, 475.7)	18.3	(2.3, 143.6)