

Title: Subsequent Meningiomas in Survivors of Childhood Cancer: a Report from the Childhood Cancer Survivor Study (CCSS)

Authors: Tab Cooney, Yan Chen, Yan Yuan, Robert Galvin, Wendy Leisenring, Susan Smith, Rebecca Howell, Michael Arnold, Miriam Conces, Daniel Bowers, Yutaka Yasui, Lisa Diller, Gregory T. Armstrong, Joseph Neglia, Lucie Turcotte

Meningiomas are the most common subsequent central nervous system tumor among aging survivors of childhood cancer, yet incidence across the lifespan, occurrence of multiple meningiomas, and risk for mortality are not established. Meningiomas were identified by self-report and validated with pathology/medical records. Twenty-year cumulative incidence of meningioma (95% confidence interval) was estimated and multivariable models assessed demographic- and treatment-related meningioma risk factors. Among 24,902 5-year survivors of childhood cancer diagnosed 1970-1999, we identified 472 survivors with 710 meningiomas, 145 (20.4%) of which were WHO grade 2/3. Among survivors with meningioma, 137 (28%) had ≥ 2 meningiomas, and 80 (16%) met criteria for meningiomatosis. The median latency from childhood cancer to first meningioma diagnosis was 26.2 years (range 5.6-48.2), and the median time from first to second meningioma (among those without meningiomatosis) was 1.4 years (range 0-30.2 years). The twenty-year cumulative incidence did not significantly decrease between survivors diagnosed in the 1970s (0.58, 95% CI 0.41-0.79) and the 1990s (0.42, 95% CI 0.32-0.55). In multivariable analysis, female sex (HR 1.52, 95% CI 1.21-1.91) and all cranial radiotherapy dose levels (>0-30Gy, HR 57.0, 95% CI 7.93-419.60; 30.1-50 Gy, HR 228.90, 95% CI 30.89-1695.99; >50 Gy, HR 113.29, 95% CI 15.09-850.34) were associated with increased meningioma risk, while older age at diagnosis (10-14 years, HR 0.60, 95% CI 0.44-0.82; 15-20 years, HR 0.35, 95% CI 0.22-0.55) was associated with reduced meningioma risk. Among 71 deaths in survivors with meningioma, the most prevalent cause of death was meningioma (N=25, 35.2%). The 5-year all-cause mortality from first meningioma diagnosis was 4.20% (95% CI: 2.44-5.96%). In conclusion, cranial radiation, younger diagnostic age and female sex were identified as independent meningioma risk factors in, to our knowledge, the largest study to date. The risk for meningioma-associated mortality argues for assertive meningioma surveillance and treatment in this population.