

## **Subsequent Neoplasms in Survivors of Central Nervous System Tumors: Risk After Modern Multi-modal Therapy**

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### **Purpose:**

To report the cumulative incidence of, and risk factors for, subsequent neoplasms (SNs) after a primary central nervous system (CNS) tumor, and determine if modern multi-modal therapy including radiation therapy (RT) plus chemotherapy increases risk for SNs.

### **Methods:**

Analysis included 2,779 patients with a primary CNS tumor treated at St. Jude Children's Research Hospital between 1985-2011. Standardized incidence ratios (SIR) for SN were calculated using age-, sex- and year-specific incidence rates. Cumulative incidence of SNs among 237 five-year survivors of medulloblastoma treated with multi-modal therapy [RT plus chemotherapy] was compared with 139 five-year survivors treated with RT alone in a historical cohort (Childhood Cancer Survivor Study).

### **Results:**

81 survivors had 97 SNs. Cumulative incidence of SNs was 3.0% (95% Confidence Interval [CI] 2.3-3.9) at 10 years, and 6.0% (95% CI 4.6-7.7) at 20 years from diagnosis. SIRs were highest for subsequent acute myeloid leukemia (453.7, 95% CI 146.2-1059), glioma (69.6, 95% CI 44.1-104.5), and soft tissue sarcoma (36.1, 95% CI 13.2-78.7). Compared to glioma, survivors of medulloblastoma (hazard ratio [HR] 4.1, 95% CI 2.2-7.7) and ependymoma (HR 3.3, 95% CI 1.6-6.8) had significantly increased risk for SNs. Compared to RT alone, risk of SN was 1.02 (95% CI 0.39-2.37) for chemotherapy only and 0.65 (95% CI, 0.39-1.08) for RT plus chemotherapy. Among five-year survivors of medulloblastoma treated with multi-modal therapy, cumulative incidence of SNs was 5.5% (95% CI 2.8-9.6%) at 10 years, and 12.0% (95% CI 6.4-19.5%) at 20 years. Medulloblastoma survivors treated with RT plus chemotherapy, when compared to those treated with RT alone, demonstrated no increased incidence of SNs at 20 years (12.0% vs. 11.3%, p=0.44).

### **Conclusion:**

Survivors of childhood CNS tumors continue to experience SNs decades following diagnosis, but with long-term follow-up the increased risk is not higher with multi-modal therapy compared to RT alone.