Radiation-induced cognitive impairment--from bench to bedside.

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Abstract
Approximately 100,000 patients per year in the United States with primary and metastatic brain tumor survive long enough (>6 months) to develop radiation-induced brain injury. Before 1970, the human brain was thought to be radioresistant; the acute central nervous system (CNS) syndrome occurs after single doses of ≥ 30 Gy, and white matter necrosis can occur at fractionated doses of ≥ 60 Gy. Although white matter necrosis is uncommon with modern radiation therapy techniques, functional deficits, including progressive impairments in memory, attention, and executive function have become increasingly important, having profound effects on quality of life. Preclinical studies have provided valuable insights into the pathogenic mechanisms involved in radiation-induced cognitive impairment. Although reductions in hippocampal neurogenesis and hippocampal-dependent cognitive function have been observed in rodent models, it is important to recognize that other brain regions are affected; non-hippocampal-dependent reductions in cognitive function occur. Neuroinflammation is viewed as playing a major role in radiation-induced cognitive impairment. During the past 5 years, several preclinical studies have demonstrated that interventional therapies aimed at modulating neuroinflammation can prevent/ameliorate radiation-induced cognitive impairment independent of changes in neurogenesis. Translating these exciting preclinical findings to the clinic offers the promise of improving the quality of life in patients with brain tumors who receive radiation therapy.