

Radiation-induced cognitive impairment in older adults

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Clinical question

One of my older patients is considering brain radiation therapy. How can I help them?

Bottom line

Approximately 70% of all cancers occur in patients aged 65 years or older,¹ and as the population ages the incidence of cancers involving the brain is expected to increase.² Neurotoxicity—from radiotherapy alone or when combined with systemic therapies—is more frequently experienced by older adults.³ Patients need to be aware of possible side effects to be able to make informed decisions about treatment.⁴ Recognizing subtle or late side effects of treatment is also important. Family physicians can help patients and their families plan discussions about treatment with their oncologists. This paper summarizes key points from an article published in the *Canadian Geriatrics Society Journal of CME*.⁵

Evidence

- Radiation-induced brain injury (RIBI) is a syndrome of functional and anatomic deficits postradiotherapy for brain lesions. It is a well-established side effect of radiotherapy in cancer patients and is more commonly seen in older adults.⁶ The 3 phases of RIBI are acute, early delayed, and late delayed.
- Acute changes are noted within days of treatment and are often transient.⁶ Patients present with headache and drowsiness related to cerebral edema and disruption of the blood-brain barrier.⁷
- Early delayed RIBI can involve transient demyelination. It develops within weeks to 6 months after treatment and is usually reversible. It may present as somnolence, attention deficits, and memory loss.⁶
- Late delayed changes develop 6 months or longer after treatment and are often progressive and irreversible.⁶ This form of RIBI manifests as radiation-induced cognitive impairment owing to white matter necrosis, permanent demyelination, gliosis, vascular abnormalities, and hippocampal injury.⁷
- Radiation-induced cognitive impairment is a concerning side effect of radiotherapy in patients with primary and secondary brain cancers.^{3,8} The main cognitive domains affected are memory, executive function, attention, and visuomotor speed related to radiotherapy-induced frontal and subcortical dysfunction.⁸

Approach

Determine whether your patient is a good candidate for brain radiation. Patients can be assessed using the Clinical Frailty Scale, with lower scores representing better functioning: scores 1 to 3 indicate individuals are fit or managing well, scores 4 to 6 indicate they are living with mild to moderate frailty, and scores 7 to 9 indicate they are living with severe frailty or are terminally ill.⁹ Fit older patients should be offered the same treatment as younger patients. Individuals with mild to moderate frailty should have modifiable factors addressed to try to optimize their health and may require treatment modifications. Patients with severe frailty should receive optimized supportive care. Additional information on assessment and management of older adults with cancer can be found in the 2019 Geriatric Oncology Conference report.¹⁰

Clinicians should perform baseline and longitudinal follow-up assessments to review cognition before and after the start of treatment. This will help identify whether cognitive impairment is present before treatment and determine specific domains affected by other conditions, by the cancer, or by radiation treatment.

Implementation

Options for mitigating risk of radiation-induced cognitive impairment. Whole-brain radiation therapy remains a crucial strategy in the treatment of multiple brain metastases as it targets the entire brain, including microscopic lesions. Radiation-induced cognitive impairment may be seen, particularly when radiating frontal and subcortical areas of the brain,³ where injuries can affect executive function, visuomotor speed, and attention, and in the hippocampus, where radiation can affect memory and learning. Because of potential for neurotoxicity, alternatives to whole-brain radiation therapy can be considered and are summarized in **Table 1**.^{11,12}

Not every person receiving radiation treatment will develop RIBI; concerns must be weighed against the natural history of brain lesions and outcomes associated with not treating. However, raising these issues with older patients who are considering brain radiation can contribute to more meaningful discussions with their oncologists and lead to more fully informed decisions. Recognizing side effects earlier can help guide care and improve outcomes of treatment.



Table 1. Brain-related radiotherapy techniques

RADIOTHERAPY TECHNIQUE	DEFINITION
Whole-brain radiation therapy	Radiotherapy that targets the entire brain, treating even microscopic, nonvisible lesions. Usually consists of 5 to 15 sessions of radiotherapy ¹¹
Brain SRS, SABR, FSRT	Personalized, highly precise radiation delivered directly to visible cranial targets. This approach uses a high dose of radiation in a single session (SRS) or a few sessions (SABR), or it uses a regular dose but with high-precision (FSRT) delivery ¹²
Gamma knife	Delivers SRS using gamma rays from a cobalt radioactive source
CyberKnife	Delivers SRS, SABR, and FSRT using x-rays from a robotic linear accelerator
X-knife	Delivers SRS, SABR, and FSRT using x-rays from a conventional linear accelerator
Intensity-modulated radiotherapy and simultaneous integrated boost	Differential radiation doses per session delivered to selected regions during the same treatment session, leading to different total doses given to targets in the same number of sessions ¹²
FSRT—fractionated stereotactic radiotherapy, SABR—stereotactic ablative radiotherapy, SRS—stereotactic radiosurgery.	

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Competing interests

None declared

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Can Fam Physician 2023;69:262-3. DOI: 10.46747/cfp.6904262

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Geriatric Gems are produced in association with the *Canadian Geriatrics Society Journal of CME*, a free peer-reviewed journal published by the Canadian Geriatrics Society (<http://www.geriatricsjournal.ca>). The articles summarize evidence from review articles published in the *Canadian Geriatrics Society Journal of CME* and offer practical approaches for family physicians caring for elderly patients.