

# Radiotherapy

## Clinical pearls for primary care

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Family physicians play an integral role in the management of their patients with cancer. At least 50% of cancer patients will undergo radiation therapy at some point during their illness trajectory.<sup>1</sup> This article summarizes the basic principles, techniques, indications, and side effects (SEs) of radiotherapy.

Ionizing radiation causes damage to DNA and other critical machinery of rapidly dividing cells, resulting in cell death and tumour shrinkage.<sup>2</sup> The unit of measurement for radiation is the gray (Gy), which is equal to 1 joule of absorbed energy per kilogram of tissue. The total planned radiation dose is divided into multiple sessions, referred to as *fractions*, to optimize malignant cell damage while minimizing toxicity to normal tissues and organs.

### Treatment techniques

Radiotherapy can be delivered using an external source (external beam radiotherapy [EBRT]), an internal source (brachytherapy), or by intravenous administration of radioisotopes that are selectively absorbed by the targeted tissue. The most common form of radiotherapy is EBRT, which is delivered by a linear accelerator. These machines use sophisticated software systems to direct x-rays (photons) or electrons to a target. The first step in preparing for EBRT is a simulation session. This process involves imaging, usually computed tomography or magnetic resonance imaging; applying markings or tattoos to assist in landmarking the patient's position; and immobilization with various devices (thermoplastic shells, wedges, bite blocks) on the treatment table. The radiation oncologist and physicists then create a treatment plan that will specify the volume of tissue to be treated, the dose to be delivered, and the number of fractions required to safely deliver this dose.

To maximize the dose to the target and minimize exposure of normal tissue, radiation beams are delivered from several directions to match the target volume as closely as possible in a process known as *conformal radiotherapy*. Image-guided and intensity-modulated radiotherapy use 3-dimensional imaging to allow multiple regions within the target to be treated simultaneously with different dose intensities.<sup>3-5</sup> Machines with these capabilities can perform stereotactic body radiotherapy and stereotactic radiosurgery, in which high-intensity radiation is delivered in just a few fractions. A linear accelerator mounted on a robotic arm (CyberKnife; Accuray Inc) has the added function of motion tracking using real-time imaging to adjust for breathing and other involuntary movements during treatment to sites

such as the brain, spine, thorax, abdomen, and prostate, where the risk of damage to adjacent tissue is high.<sup>6</sup>

External beam radiotherapy treatments are usually split into daily fractions that are given Monday to Friday, or occasionally twice daily or once weekly. The treatment itself takes minutes to deliver but the whole process, including positioning, takes 15 to 30 minutes. A typical curative regimen delivers a total dose ranging from 40 to 80 Gy given over 3 to 8 weeks. Hypofractionation trials have demonstrated that the total dose can be safely given in fewer fractions while achieving similar response rates.<sup>7</sup> This has improved resource use and has been pivotal in decreasing the frequency of visits to cancer centres during the coronavirus disease 2019 pandemic.<sup>8</sup> For example, the treatment of prostate cancer can be decreased from 7 or 8 weeks to 4 weeks, and breast cancer treatment can be reduced from 5 weeks to 3 weeks.<sup>9,10</sup>

### Indications

Curative radiotherapy (given as monotherapy or concurrently with chemotherapy in the neoadjuvant or adjuvant setting) has a high risk of SEs and complications, and so the patient's overall health and comorbidities must be carefully considered and balanced with the chance of cure. Conversely, palliative radiation is intended to provide rapid symptom relief, and late toxicity is less of a concern. For this reason, larger doses are often given as a single fraction or over a few days rather than weeks (**Table 1**).<sup>2</sup>

Family physicians should be aware of the indications for palliative radiation therapy, as it is an effective tool in the provision of palliative care (**Table 2**).<sup>11-19</sup> The therapeutic effects of radiation are not immediate and the time to response varies from 1 to 4 weeks; patients being considered for palliative radiation should have a life expectancy of at least 1 month.<sup>20,21</sup> Most cancer centres have rapid palliative radiation referral programs that facilitate access to treatment, with wait times of only 2 to 3 days, and same-day assessment and treatment.<sup>22</sup>

### Treatment-related SEs and their management

Although technical advancements have contributed to reducing radiotherapy-related toxicity,<sup>23</sup> many patients remain afflicted with taxing SEs.<sup>24</sup> Side effects are classified as early or late, the former presenting during or within weeks of radiotherapy completion, and the latter manifesting months to years thereafter.<sup>24</sup>

Side effects can be psychological or physical in nature. Psychological SEs include distress, anxiety, and

**Table 1.** Typical curative vs palliative radiotherapy dosing regimens: *Many different treatment schedules exist, and regimens vary depending on the neoadjuvant vs adjuvant setting; use of radiation alone vs radiation and chemotherapy; tumour stage, size, and location; and technique employed.*

MALIGNANCY	CURATIVE TREATMENT DOSE	PALLIATIVE DOSE
GBM	60 Gy/30 fractions, 40 Gy/15 fractions*	25 Gy/5 fractions
Brain metastasis (whole brain radiation)	NA	20 Gy/5 fractions, 30 Gy/10 fractions
SCLC (prophylactic cranial irradiation)	25 Gy/10 fractions	NA
Brain metastasis (SRS)	NA	15-24 Gy/1-3 fractions
Head and neck	70 Gy/35 fractions	30 Gy/10 fractions, 8 Gy/1 fraction
Lung, stage I to II (SBRT)	54-60 Gy/3-8 fractions	NA
Lung, stage III	60 Gy/30 fractions	30 Gy/10 fractions
Esophagus	50 Gy/25 fractions	30 Gy/10 fractions
Breast	50 Gy/25 fractions, 40 Gy/15 fractions	NA
Prostate	70 Gy/35 fractions, 60 Gy/20 fractions	NA
Rectum	45 Gy/25 fractions, 50 Gy/30 fractions	25 Gy/5 fractions
Bone metastasis	NA	800 cGy/1 fraction or 20 Gy/5 fractions
Spinal cord compression	NA	800 cGy/1 fractions or 20 Gy/5 fractions
SVCO	NA	20 Gy/5 fractions

\*Radical treatment for GBM (treatment for GBM is not curative).  
 NA—not applicable, GBM—glioblastoma multiforme, SBRT—stereotactic body radiotherapy, SCLC—small cell lung cancer, SRS—stereotactic radiosurgery, SVCO—superior vena cava obstruction.  
 Data from Gunderson and Tepper.<sup>2</sup>

**Table 2.** Palliative indications for radiation oncology referral

INDICATIONS	PATIENTS WITH RESPONSE TO TREATMENT
Pain from bone metastases	60%-88% partial relief, 17%-24% complete relief <sup>11</sup>
Spinal cord compression symptoms	
• Weakness or loss of motor function	60% <sup>12</sup>
• Pain or reducing analgesic use	61.9% <sup>12</sup>
Hemoptysis	86% <sup>13</sup>
Gastric bleeding	69% <sup>14</sup>
Hematuria	57%-72% <sup>15</sup>
Vaginal bleeding	100% <sup>16</sup>
Rectal bleeding	89% <sup>16</sup>
Overall primary bleeding control rate	89% <sup>16</sup>
Dyspnea or airway obstruction, cough	66%, 71% <sup>13</sup>
Superior vena cava obstruction	83%-86% <sup>17</sup>
Obstruction	
• Dysphagia, or gastric outlet, biliary, or rectal obstruction	35%-45% <sup>18</sup>
Brain metastases	
• Physical condition	37% <sup>19</sup>
• Global health status	82% <sup>19</sup>

depression, and must not be overlooked.<sup>25</sup> Distress screening using the Edmonton Symptom Assessment System–Revised, distress thermometer, or Patient Health Questionnaire–2,<sup>25</sup> and prompt care and referrals for psychosocial issues are key components of management.<sup>25</sup> Moreover, family physicians should rule out potentially contributing causes, including radiotherapy-induced hypothyroidism and vitamin B12 malabsorption.<sup>26</sup>

Physical SEs include cancer-related fatigue; skin SEs; head and neck SEs; and cardiac, pulmonary, gastrointestinal, or sexuality-related SEs (Table 3).<sup>27</sup> Cancer-related fatigue affects nearly 80% of patients who receive chemotherapy and-or radiotherapy; the mainstay of management is nonpharmacologic, with patient support, physical exercise, yoga, acupuncture, cognitive-behavioural therapy, and other mindfulness-based therapies.<sup>28</sup> In refractory cases, methylphenidate might be considered; modafinil is not recommended.<sup>28</sup> Moreover, potential contributing factors, such as anemia and cardiac or endocrine abnormalities, should be readily managed.<sup>28</sup>

Radiation dermatitis is a common skin radiation-related SE observed in the head and neck, breast, vulva, and anorectal areas owing to the proximity to the skin surface. The severity of the reaction is dose dependent. Loose clothing and avoidance of perfumes or harsh soaps are recommended general measures to aid in skin preservation. Protective spray-on barrier films might be useful in delaying the onset and minimizing the

**Table 3. Radiotherapy side effects**

LOCATION	ACUTE	SUBACUTE	LATE
General	<ul style="list-style-type: none"> <li>• Fatigue</li> </ul>		<ul style="list-style-type: none"> <li>• Second malignancy in the field of radiation (&lt; 1% risk in older adults; higher risk in pediatric or younger populations)</li> </ul>
Skin	<ul style="list-style-type: none"> <li>• Sunburned appearance (erythema, pruritus)</li> <li>• Dry skin peeling (or dry desquamation)</li> <li>• Weeping skin (or wet desquamation)</li> <li>• Ulceration and bleeding (rare)</li> </ul>		<ul style="list-style-type: none"> <li>• Decreased sweating</li> <li>• Hair loss</li> <li>• Tanning (hyperpigmentation or hypopigmentation)</li> <li>• Telangiectasia</li> <li>• Fibrosis</li> </ul>
Lung	<ul style="list-style-type: none"> <li>• Cough</li> </ul>	<ul style="list-style-type: none"> <li>• Radiation pneumonitis (syndrome of cough, dyspnea, hypoxia, fever, radiologic changes)</li> </ul>	<ul style="list-style-type: none"> <li>• Reduced pulmonary function</li> </ul>
Heart	<ul style="list-style-type: none"> <li>• No specific acute or subacute effects</li> </ul>		<ul style="list-style-type: none"> <li>• Coronary artery disease</li> <li>• Pericarditis</li> </ul>
Head and neck	<ul style="list-style-type: none"> <li>• Mucositis</li> <li>• Xerostomia (dry mouth)</li> <li>• Dysphagia</li> <li>• Odynophagia</li> <li>• Weight loss (from poor nutritional intake)</li> </ul>		<ul style="list-style-type: none"> <li>• Dysphagia or odynophagia</li> <li>• Dysgeusia (changes in taste)</li> <li>• Voice changes</li> <li>• Dental complications</li> <li>• Osteonecrosis of the mandible (rare)</li> </ul>
Esophagus	<ul style="list-style-type: none"> <li>• Esophagitis</li> <li>• Nausea</li> <li>• Anorexia</li> </ul>		<ul style="list-style-type: none"> <li>• Esophageal perforation (rare)</li> <li>• Tracheoesophageal fistula (rare)</li> <li>• Esophageal stricture (rare)</li> </ul>
Small and large bowel	<ul style="list-style-type: none"> <li>• Nausea and vomiting</li> </ul>		<ul style="list-style-type: none"> <li>• Radiation colitis (rare)</li> </ul>
Anorectal	<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Mucus discharge from the rectum</li> </ul>	<ul style="list-style-type: none"> <li>• Radiation proctitis (rare)</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic bowel habit change</li> <li>• Rectal urgency</li> <li>• Fistulae, strictures, obstructions (rare)</li> </ul>
Bladder and prostate	<ul style="list-style-type: none"> <li>• Irritative or obstructive urinary symptoms</li> <li>• Sexual dysfunction</li> <li>• Radiation cystitis (rare)</li> <li>• Urethra stricture (rare)</li> </ul>		
Vagina	<ul style="list-style-type: none"> <li>• Vaginitis (irritation)</li> </ul>		<ul style="list-style-type: none"> <li>• Vaginal stenosis</li> <li>• Fistula (rare)</li> </ul>
Ovary	<ul style="list-style-type: none"> <li>• No specific acute or subacute effects</li> </ul>		<ul style="list-style-type: none"> <li>• Induced menopause</li> <li>• Infertility</li> </ul>
Brain	<ul style="list-style-type: none"> <li>• Increased ICP</li> <li>• Headache</li> <li>• Seizures</li> <li>• Nausea and vomiting</li> </ul>	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Cognitive decline</li> <li>• Cataracts (lens effects)</li> <li>• Hearing loss (cochlear effects)</li> <li>• Hormonal imbalance (pituitary or hypothalamic effects)</li> </ul>	
Bone	<ul style="list-style-type: none"> <li>• Marrow suppression</li> <li>• Pain flares</li> </ul>		<ul style="list-style-type: none"> <li>• Fracture due to osteopenia</li> <li>• Bone growth arrest (pediatric)</li> </ul>

ICP—intracranial pressure.  
Adapted from Ingledew et al.<sup>27</sup>

severity of skin reactions.<sup>29</sup> Skin irritation associated with erythema and dry desquamation is managed with weak topical steroids (1% hydrocortisone) and moisturizers (glaxal base), whereas moist desquamation often requires the use of antibacterial creams such as silver sulfadiazine or bacitracin–polymyxin B.<sup>30,31</sup> In the anogenital area, saline or aluminum acetate solution soaks and sitz baths are recommended.

Head and neck radiotherapy SEs include oral mucositis, taste alterations, xerostomia, hypothyroidism, dysphagia, and lymphedema. Cancer Care Ontario and BC Cancer provide easy-to-use clinical guidelines on how to address these frequent SEs (**Box 1**).<sup>32–36</sup> Radiation to the head and neck can also lead to carotid artery stenosis, thereby increasing cerebrovascular disease risk. Family physicians therefore have a crucial role in screening for

**Box 1. Radiotherapy side effect resources**

## Head and neck side effects

- Cancer Care Ontario<sup>32</sup>: <https://www.cancercareontario.ca/en/symptom-management/3156>
- BC Cancer<sup>33</sup>: <http://www.bccancer.bc.ca/patient-and-public-info-site/Documents/RT%20Side%20Effects%20Education%20Materials/Care-of-Radiation-Therapy-Side-Effects-Head-and-Neck.pdf>

Cancer-related lymphedema<sup>34</sup>

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7755442/pdf/conc-27-336.pdf>

Radiation-induced lung injury<sup>35</sup>

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8097634/pdf/main.pdf>

Pelvic radiation disease<sup>36</sup>

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7253739/table/tIII-conc-27-107/?report=objectonly>

Overview of common radiotherapy side effects and their management<sup>36</sup>

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7253739/>

and managing comorbid conditions including smoking, diabetes, dyslipidemia, and coronary and peripheral artery diseases.<sup>37</sup>


Thoracic radiotherapy can cause radiation-induced lung injury and radiation-induced heart disease. Radiation-induced lung injury can present as dyspnea and lead to lung fibrosis, adversely affecting quality of life.<sup>38</sup> Radiation-induced lung injury comprises an acute inflammatory phase and a chronic fibrotic phase, the former referred to as *radiation pneumonitis* (occurs within 3 months after radiotherapy) and the latter known as *radiation fibrosis*.<sup>39</sup> Clinical presentation often features dyspnea, dry cough, and occasionally fever, but physical examination findings are typically unremarkable.<sup>39</sup> Family physicians must consider radiation-induced lung injury in their differential diagnosis. Symptomatic patients can be treated with steroids.<sup>39</sup> Radiation-induced heart disease can occur years after radiotherapy and presents as pericardial disease, cardiomyopathy, valvular disease, coronary artery disease, or conduction anomalies.<sup>40</sup> Primary and secondary prevention measures are the cornerstone of care and include screening for and management of cardiovascular disease risk factors (diabetes, hypertension, obesity, dyslipidemia, smoking).<sup>41</sup> A baseline echocardiogram 6 to 12 months after radiotherapy and referral to a cardiologist might also be indicated.<sup>41</sup>

Pelvic cancers are treated with radiotherapy more than any other cancer site, and can result in gastrointestinal toxicity, sexual issues, and fertility concerns. Pelvic radiation disease (PRD) refers to mild to severe temporary

or long-term gastrointestinal symptoms that can substantially impact quality of life.<sup>42</sup> Given frequent non-PRD-specific gastrointestinal symptoms including urgency, diarrhea, and rectal bleeding can occur, systematic investigation is recommended.<sup>43</sup> Of note, sucralfate, amino-salicylates, corticosteroid enemas, bile acid sequestrants, selenium, famotidine, and dietary modifications have less evidence for potential benefit in PRD management.<sup>44</sup>

Vaginal dryness and stenosis, decreased libido, dyspareunia, and erectile dysfunction can arise owing to pelvic radiation and can negatively impact intimacy and self-esteem.<sup>45</sup> Nonhormonal lubricants may help with vaginal dryness experienced during intercourse.<sup>45</sup> Vaginal dilators and pelvic physiotherapy might improve vaginal elasticity.<sup>45</sup> Erectile dysfunction can be treated with phosphodiesterase 5 inhibitors.<sup>46</sup> Intimacy and self-esteem issues can also result from radiotherapy-induced bladder or bowel dysfunction.<sup>46</sup> Family physicians should screen for intimacy and sexual concerns and refer patients to a psychologist or sex therapist when warranted.<sup>46</sup> Finally, as pelvic radiotherapy might increase the risk of preterm labour, spontaneous miscarriages, low birth weight, and placental anomalies, close pregnancy monitoring by a multidisciplinary team is indicated.<sup>47</sup> Key resources for management of common radiotherapy SEs are presented in **Box 1**.<sup>32-36</sup>

**Conclusion**

Radiotherapy is widely used for the curative and palliative treatment of malignancies. Family physicians are well suited to screen for and address radiotherapy-related SEs and complications, manage underlying comorbid conditions, and promote healthy lifestyle habits in cancer survivors. 

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**Competing interests**

None declared

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