Radiation Therapy

Contents

Introduction

Radiation therapy (radiotherapy or RT) is used either alone or in combination with surgery or systemic cancer drug therapy. During RT, high energy particles (X-rays, gamma rays, electron beams, protons, or radioactive molecules) are delivered to a target area at a set dose. This damages the DNA of cancer cells, which are more susceptible to RT than normal cells, and can lead to shrinkage or elimination of the tumour. When given with palliative intent, RT is used to relieve symptoms such as bone pain and improve patient's quality of life.

Below are a number of reasons for RT administration:

- to shrink bulky tumour before surgery (neoadjuvant)
- to stop growth of any remaining cancer cells after surgery (adjuvant)
- to treat a tumour in an unfavourable location
- to eradicate cancer cells in multiple, large lymph nodes
- to alleviate symptoms caused by tumours or metastases.

Types of Radiation Therapy

Radiation therapy is administered only at BC Cancer Centres in BC, and can be delivered as:

- external beam radiation therapy
- internal beam radiation therapy or brachytherapy
- systemic radiation

External Beam Radiation Therapy

External beam radiation therapy (EBRT) is given using a linear accelerator. There are many different types of external beam radiation treatments given at BC Cancer. Treatment may be given over a single session, multiple sessions, or more frequently at 5 days a week for several weeks. Treatment is targeted to minimize dose-limiting damage to the surrounding healthy tissues and organs (organs at risk). EBRT types include the following:

3D Conformal Radiation Therapy (3DCRT)

3DCRT is given to closely fit the treatment area. Several radiation beams of *same* intensity follow a 3D image of the tumour to deliver RT to the precise location, while avoiding the surrounding healthy tissue.

Intensity Modulated Radiation Therapy (IMRT)

In IMRT, the shape of the radiation field changes as it is delivered to the treatment area. Several radiation beams of *different* intensity are used to follow a 3D image of the tumour and deliver RT to the precise location. The radiation field is shaped to provide a higher RT dose to the tumour, while sparing the surrounding normal tissue from damage. IMRT can be used to treat hard to reach tumours such as those in head, neck, spine, brain, lung, and prostate.

Volumetric Modulated Arc Therapy (VMAT)

VMAT is an advanced form of IMRT, where the machine moves around the patient in a circle (360-degree rotation) to allow for further shaping of the radiation field.

Stereotactic Radiation Therapy

In stereotactic RT, higher doses of radiation are delivered to the target area of the body or brain over a shorter treatment period than IMRT.

When stereotactic RT is delivered to the body (lung, liver, bone), it is called stereotactic body radiation therapy (SBRT) or stereotactic ablative radiation therapy (SABR). SBRT is generally given in 3 to 8 total treatments/doses.

When stereotactic RT is delivered to the brain (for treating brain metastases), it is either given in a single session called stereotactic surgery (SRS), where thin radiation beams from different angles converge at the tumour site to deliver a single high dose, or over multiple sessions called stereotactic treatment (SRT) .

Internal Beam Radiation Therapy (Brachytherapy)

Internal beam radiation therapy or brachytherapy involves placement of radioactive seeds (an implant) inside a tumour. This implant provides continuous radiation to the tumour while protecting the surrounding normal cells and can either be left in the body permanently or removed after treatment is completed. This type of RT is used to treat breast, prostate, lung, sarcoma, head and neck, and colorectal cancers.

Intracavitary brachytherapy

Implant is placed inside the body cavity – used generally in gynecological cancers.

Interstitial brachytherapy

Implant is placed right inside the tumour, generally used in prostate or head and neck tumours. It can be given in conjunction with EBRT.

Intraluminal or transluminal brachytherapy

Implant is placed inside a body passage – used generally in esophageal cancers. It can be given in conjunction with EBRT.

Plaque or surface brachytherapy

A very small implant is placed on the surface of a tumour – used generally for eye or skin cancers.

Brachytherapy Dosing

Brachytherapy may be given as high-dose-rate (HDR) or low-dose-rate (LDR).

In HDR, a single high dose of radiation is delivered in a very short period of time using tubes or needles inserted into the tumour. Once treatment is finished (usually only a few minutes long), the radioactive material is removed from the patient's body. It can be delivered as a single dose or multiple doses.

In LDR, continuous low doses of radiation are delivered over hours or days using an implant containing radioactive material (permanent seed implants). Patients with prostate cancer have the Iodine-125 seeds implanted using this technique.

Precautions:

- Children under 10 years of age should not sit on the lap of the patient for the first 2-4 months after the implant. They can sit next to the patient.
- Prolonged contact with pregnant women should be avoided for the first 2-4 months after the implant. Patient should stay at least 2 meters (6 feet) away from pregnant women.

Systemic Radiation

Systemic radiation involves the use of radioactive drugs (radiopharmaceuticals) to treat cancers such as thyroid cancer and bone metastases from prostate cancer. These drugs are formulated as an oral capsule or injectable liquid that contains a radioactive substance that is administered orally or parenterally. The radioactive drug generally concentrates in areas where cancer cells are found, making it a useful tool to locate the tumour or metastases. **Radiopharmaceuticals are not handled by BC Cancer Pharmacies.** They are typically provided by nuclear medicine departments.

Thyroid Cancer

Systemic radiation is used for patients whose thyroid cancer has spread to other parts of the body, especially lymph nodes or the neck region. It is also used for patients who have undergone partial or complete thyroidectomy, to eliminate any remaining cancer cells or diagnose recurrence of thyroid cancer.

Patients are treated with an oral capsule of traditional radioactive iodine, radioiodine I-131, to destroy thyroid cells. Both healthy and cancerous thyroid cells preferentially absorb radioactive iodine which causes thyroid ablation. Unabsorbed radioiodine I-131 is eliminated through urine within 2-3 days after the treatment. Therefore, patients may be admitted to hospital for a few days until no radioactive substances are excreted through urine in order to minimize exposure to family members. The half-life of radioiodine I-131 is 8 days.

Patients who have undergone partial or complete thyroidectomy or thyroid ablation are given levothyroxine for thyroid replacement to avoid hypothyroidism and keep thyroid stimulating hormone (TSH) levels within normal range. Since high levels of TSH are needed for thyroid tissue and thyroid cancer cells to absorb radioiodine I-131, patients can **either** hold levothyroxine for 2 weeks prior to scanning/treatment **or** receive the recombinant form of TSH (thyrotropin alpha). This is given intramuscularly – one dose once daily for two days (see HNOTTSH protocol). If thyrotropin alpha is used, the patient does not have to hold levothyroxine and risk hypothyroidism symptoms. Information on serum thyroglobulin (Tg) and TSH testing can be found in the BC Cancer Drug Manual monograph for thyrotropin alpha.

Bone Metastases from Prostate Cancer

In patients with hormone resistant metastatic prostate cancer with multiple bone metastases, systemic radiation in the form of radioactive strontium (Sr-89) is used at BC Cancer. Sr-89 is chemically similar to calcium and is therefore preferentially taken up by osteoblasts. Unabsorbed Sr-89 is eliminated through urine within 2-3 days after the injection. Therefore, patients are admitted to hospital for a few days until no radioactive substances are excreted through urine in order to minimize exposure to family members. The half-life of Sr-89 is 50.5 days.

Radiation Therapy Treatment Planning

Simulation

Prior to starting RT, patients undergo RT planning and simulation where the patients are positioned on the simulation table and a CT simulator is used to take 3D images of the area to be treated. These images help the RT team to decide where and how to deliver radiation. The position in which the patient will receive their radiation treatment is also determined during this visit. Once decided, the patient receives treatment in the same position each time. In order to deliver RT to precisely the same area each time, items such as skin markings (temporary or permanent tattoos) or head immobilization masks are used. Skin markings act as a map of where the radiation beam is targeted during treatment. Similarly, the masks, which are custom made for each patient, are used to immobilize the target area and may also contain markings to help direct the radiation beams.

Dose and Schedule

The dose of radiation is calculated based on the tumour characteristics such as type of cancer, radiosensitivity of the tumour, size and location of the tumour, and size of area that needs to be irradiated. The dose is measured in units called **grays** (Gy) or **centigrays** (cGy). Note: some body areas such as the spinal cord and brainstem can only receive a certain amount of radiation over a patient's lifetime. Once an area has received the maximum dose, no further radiation can be given to that area. The maximum dose depends on the body area being treated.

Some treatments are given over one day, while others can be delivered over weeks, generally on weekdays with breaks over weekends and statutory holidays. Palliative intent RT is delivered over a few days up to 2 weeks. When delivered as a single dose, RT is called stereotactic radiosurgery, and is generally used in brain metastases. When delivered as a small dose (dose per fraction) over a period of time (generally 5 to 7 weeks), it is called fractionated radiotherapy.

Fractionated radiotherapy can be delivered following a number of different schedules:

Accelerated fractionation

The daily dose of radiation is given over multiple sessions per day to allow for a shorter total duration of therapy.

Hyperfractionated radiotherapy

The total dose of radiation is divided into smaller increments which are given over multiple sessions per day. This allows for a larger dose to be tolerated over the same total time period.

Hypofractionated radiotherapy

The total dose of radiation is divided into larger increments which are given once a day or less often. This allows for the delivery of higher dose-per-fraction treatment over a shorter period of time (usually 4 weeks).

Radiation boost

Additional RT is given to a smaller area after regular radiation treatment is completed.

Radiation Induced Toxicities

Radiation therapy can cause toxicities in the target organ and the surrounding tissues. Some toxicities can develop immediately after RT while others can develop months to years after receiving RT. Note: when RT is delivered to a large surface area of the body or to a location with large bone marrow reserve (e.g., long bones), the immunosuppressive side effects can be long lasting. This prior radiotherapy can impact toxicity in future chemotherapy treatments (see *Dual Modality Protocols*).

Early RT Toxicities

Generally, RT can cause irritation and edema in targeted tissues leading to acute side effects limited to the area. For example abdominal irradiation may cause nausea and vomiting, head and neck irradiation may cause mucositis, and pelvic irradiation may cause incontinence or diarrhea. These side effects can happen during or after RT and can be short-term or can persist for a few weeks after treatment is completed.

The most common early side effects from RT include:

- skin problems
- fatigue
- difficulty eating
- nausea
- diarrhea
- pain
- hair loss at the irradiated site

These early side effects typically resolve as the localized tissue irritation and edema resolve.

Late RT Toxicities

Later side effects from RT are mostly due to fibrosis in the irradiated tissue areas. These can appear months or years after treatment is completed and depend on the area irradiated and the RT dose delivered. Additionally, secondary cancers at the irradiated site and other non-oncologic complications, such as infertility and cardiac toxicity, may develop years after a patient has had RT. See Table 1 for more examples of early and late radiation-induced toxicities.

Rarely, radiation recall dermatitis has been reported when treating patients who have received prior radiotherapy with subsequent systemic drug therapy. Radiation recall is an acute, localized, inflammatory skin reaction that flares up in the previously irradiated areas. It is thought to be triggered by the subsequent drug therapy, can occur months to years after RT exposure, and seems to be drug-specific for individual patients. It is still not well understood.

Table 1: Examples of Early and Late RT related toxicities

Site/system	Early Toxicity	Late Toxicity
Blood vessels	Vascular stenosis	Vascular wall calcifications, Vascular occlusion, Pseudoaneurysms
Bones	Bone edema and Osteopenia	Pathologic bone fractures, Osteochondromas, Osteoradionecrosis, Bone malignancy
Breast	Diffuse skin thickening	Fibrosis, Fat necrosis, Dystrophic calcifications, Skin retraction, Breast cancer
Gastrointestinal	Diarrhea, Enteritis, Hemorrhoids, Ulceration, Dismotility, Perforation	Stricture, Ulceration, Perforation, Fistulas
Genitourinary	Acute radiation cystitis, Increased urinary frequency and urgency	Hematuria, Bladder/ Ulceraction, Stone formation, Infertility
Heart	Pericardial effusion	Coronary artery disease, Chronic pericarditis, Cardiomyopathy
Liver	Focal hepatitis	Atrophic liver changes
Lungs	Infection, Radiation-induced organizing pneumonia	Tumour Recurrence
Lymph nodes	n/a	Calcified lymph nodes, fibrotic mass
Pleura	Pleural effusion	n/a
Skin	Pruritis, Dermatitis, Desquamation	Atrophy, Scarring, Telangiectasias

Management

Education for patients undergoing RT is provided by radiation therapy program nurses. Symptom management care is provided by the radiation therapy program, and most supportive care prescriptions written by radiation oncologists are filled at retail pharmacies in BC. Note: an exception is dexamethasone under the MODEXA protocol, where it is prescribed in a tapering dose for cerebral edema or CNS swelling during and following radiation therapy.

BC Cancer's Radiation Therapy Program has patient education handouts for skin care, general RT side effects, and site specific treatment side effects. Additionally, BC Cancer Nurses have specific symptom management guidelines for Radiation Dermatitis.