Principles of radiotherapy

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Radiotherapy and multidisciplinary cancer care

Radiotherapy can prolong survival, contribute to the preservation of organs affected by malignancy, provide palliation and improve patients' quality of life. Recent research shows that about 50% of patients with newly-diagnosed cancers (other than non-melanotic skin cancers) would benefit from radiotherapy[1]. One-quarter of these patients may need further treatment after relapse.

The provision of a safe and effective radiation oncology service is complex. It requires a substantial capital investment in radiotherapy equipment and specially-designed buildings, an ongoing investment in maintenance and replacement of the equipment, expert teams of doctors, therapists and physicists, and good access to engineering support.

How radiotherapy works

- Radiotherapy ionises chemicals within cells. The crucial lesion is DNA strand breakage which may be repaired or fixed and lead to apoptotic or mitotic cell death.
- Different types of normal and malignant cells vary in their susceptibility to ionising radiation. Clinical radiotherapy schedules are designed to exploit the differences between normal tissues and tumours, so that as many malignant cells as possible are killed, while damage to normal tissue is minimised. In radical curative treatments, total radiation doses are close to the tolerance of normal tissues. In palliative treatments, usually low doses are used.
- Some tumours, such as seminoma of the testis and lymphoma, are very sensitive to radiotherapy and can be treated with relatively low doses, with an expectation of cure. Other tumours, such as melanoma of the skin and glioblastoma multiforme in the brain, are notoriously resistant, even to large doses.
- A course of radiotherapy may be spread over days or weeks. This is known as fractionating, and the radiation delivered to a patient in a single treatment session is called a fraction. Fractionating allows normal tissues to repair much of the radiation damage, while tumour cells, which are less efficient at repair, do not recover. A beam of radiation is called a field. A fraction consists of one or more fields delivered sequentially.

- In general, most modern radiotherapy is delivered with very high-energy, highly-focused beams, which can reach deeper tumour tissues while depositing relatively small doses in the normal tissues through which they pass. External-beam radiotherapy can be delivered by cobalt machines or linear accelerators, collectively known as megavoltage machines.
- However, both acute (early) and late (chronic) side effects do occur. The side effects depend on several factors, including the body site being treated, the volume of normal tissue irradiated (the larger the volume, the higher the risk and severity of side effects), the total dose, and the rate of dose accumulation (the amount per week).
- Early side effects result from damage to proliferating tissues, such as the mucosa (lining) of the gastro-intestinal tract or the skin. For example, radiotherapy to an abdominal tumour may damage the mucosa of the small bowel, causing malabsorption and diarrhoea. Most patients recover completely.
- Late reactions occur at least three months after a treatment course has ended, and are usually permanent or progressive. They usually result from damage to non-proliferating differentiated tissues, which cannot compensate for cell death by dividing to replace lost cells. Once late effects occur, it is very difficult to reverse them, but they are very uncommon.
- Late effects, such as second cancers, may occur many years after treatment. Even relatively low doses of radiation may increase the risk of developing a malignancy. There is a long latent period after exposure. Leukaemia may appear up to 7 years after exposure and solid tumours may develop 10 or 20 years later.
- Side effects of radiation can be minimised by meticulous planning and delivery of a course of radiotherapy. Late-reacting tissues are particularly sensitive to the size of each radiation dose, so they can be protected to a large extent by giving small fractions of radiation, provided the total dose is not too high.

Role of radiotherapy in cancer management

Radiotherapy acts only on the irradiated tissues and can treat large areas of the body that may contain cancer. One dose of radiotherapy kills about half the cancer cells in the treated region. This powerful effect means that radiotherapy is also useful for palliation since low doses can result in significantly shrinking tumours with few side effects.

Curative radiotherapy

At least half of all patients for whom radiotherapy is prescribed, either alone or combined with surgery and/or chemotherapy, are treated with the goal of achieving a cure.

Radiotherapy is used by itself when it is the best treatment available because of the known cure rate or because it is likely to have fewer side effects. Examples include treatment for advanced cervix cancer, pituitary tumours, deep-seated gliomas and arterio-venous malformations, nasopharyngeal cancer and early stage low-grade lymphomas.

Because normal tissues recover from radiation damage better than tumours, it is possible to treat a cancer without destroying the host organ. Even if surgically removing the organ would lead to a more definite initial cure, provided radiotherapy is effective it is usually preferable so that the organ can be salvaged. Examples include larynx cancer and prostate cancer.

In the case of large tumours, radiotherapy is often combined with surgery to enable the whole tumour site to be treated without unduly affecting the patient’s ability to function normally.

In general, radiotherapy is combined with surgery when:

- organ preservation is desirable -- for example, breast conservation treatment consisting of lumpectomy and radiotherapy
- the tumour is advanced with a high risk of local recurrence after surgery, for example, after a positive neck dissection or before surgery for rectal cancer
- an inoperable cancer can be rendered operable -- for example, fixed rectal cancers
- close surgical margins need treating to prevent local recurrence.

Chemotherapy may improve the results of radiotherapy through several mechanisms outlined in Table 1.

Table 1: Beneficial interactions between radiotherapy and chemotherapy.

Mechanism	Benefits	Examples of cancer
Spatial cooperation	Radiotherapy cures the high volume local cancer and chemotherapy cures micro-metastases.	Hodgkin's lymphoma Rectal cancer
Independent toxicity	Because radiotherapy and chemotherapy have different dose limiting toxicities, it is possible to deliver a higher anti-tumour dose with fewer side-effects than with radiotherapy alone.	Cervix cancer Oesophageal cancer
Enhanced tumour response	Even if the effects of radiotherapy and chemotherapy are only additive, the steep dose response of tumours means that there can be greater rates of cure than with radiotherapy alone.	Anal cancer
Protection of normal tissues	Some dose-limiting normal tissues can be protected by chemical modifiers such as amifostine, allowing increases in the dose tolerated.	Head and neck cancers

Palliative radiotherapy

Incurable cancer causes many problems from local effects and the effects of spread to distant organs. Radiotherapy is the most effective treatment for people with incurable lung cancer. It can alleviate shortness of breath, cough and haemoptysis. It is also useful for patients with advanced and incurable cancers that are causing symptoms in the sites that they have arisen in. For breast cancer radiotherapy can control fungating masses, and for prostate cancer it can be used to relieve urinary obstruction.

Short course radiotherapy is an excellent treatment for the palliation of bone pain, brain metastases and compression of vital structures such as the spinal cord. In 80% of patients, a single dose of radiotherapy will relieve the pain caused by metastatic cancer in the bone[2]. Radiotherapy is also very effective at relieving pain from compression of nerves[3]. Radiotherapy can reverse the effects of spinal cord compression and prevent paraplegia.

Radiotherapy may be used to prolong the life of patients with incurable cancers such as high-grade gliomas. Longer courses are required so that a sufficiently high dose may be given. Radiotherapy is more effective in these cases than chemotherapy alone[4].

References

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