Principles of cancer treatment by radiotherapy

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Abstract

Radiotherapy is a component of cancer management in more than 50% of cases, and 40% of patients cured of their cancer have had radiotherapy as a part of their management. It can be used to control symptoms in patients with incurable cancer. For some patients, it can replace surgery and has the advantage of organ preservation. It is sometimes used before or after surgery to improve resection rates or to reduce recurrence rates, respectively. Outcomes may be improved if radiotherapy is combined with systemic therapies such as chemotherapy. The process of delivering radiotherapy has multiple steps and involves clinical oncologists, medical physicists and therapeutic radiographers. Each step takes advantage of new technology that allows a more accurate definition of the tumour and delivery of the radiation with the aim of improving treatment outcomes and reducing normal tissue toxicity. There have been significant advances in defining the target and delivering the radiation in the last few years and these are discussed further in this article.

Keywords Cancer; radiation; treatment

Introduction

Radiotherapy (RT) is an effective and commonly used treatment modality in cancer management. In England, 125,000 patients each year are treated with external beam radiotherapy (EBRT)[1] and it is estimated that 52% of patients with cancer receive RT at some point during their illness.[2]

The primary intent can be radical (curative) or palliative (symptom control). Forty per cent of all patients cured of their cancer have had RT as a part of their therapy, either on its own or in combination with surgery or chemotherapy.[1] Radical treatment can be as the definitive therapy (e.g. in head and neck and prostate cancers), neoadjuvant prior to definitive surgery (e.g. chemoradiotherapy for rectal cancer) or adjuvant following definitive treatment (e.g. after wide local excision of breast cancer).

Tumour types have inherently different radiation sensitivities that determine whether RT has a role in the treatment and also the dose required. Sensitive types include seminoma and lymphoma; moderately sensitive tumours are breast, lung and squamous cell carcinomas; poorly sensitive cancers include osteosarcoma and melanoma.

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Radiation therapy can be delivered in three main ways — external beam radiotherapy (EBRT) (photons/electrons/protons), implanted radioisotopes (brachytherapy) and injected radioisotopes. These are detailed in Table 1.

External beam radiotherapy

This is the most common type of RT and generally uses photons —high-energy X-rays (6—18 megavolts) that can be directed (targeted) to a specific area of the body for treatment. The photons are produced by accelerating electrons that collide with a metal target. They are delivered via a linear accelerator (Linac), which is housed in a thick walled bunker for radiation protection. The dose of radiation is defined as the energy absorbed per unit mass and is expressed in Grays (Gy) (1 Gy = 1 J/Kg). Radical RT is usually delivered in multiple treatments on a daily basis over 3—7 weeks (fractionation) depending on the dose prescribed. Fractionation is used to maximize differences in biological effects of radiation (e.g. repair and repopulation) between critical normal tissues and the cancer.

How does radiotherapy work?

The effects of radiation on tissue can be divided into four phases:

1. The physical phase — radiation absorption in tissues leads to ionization (ejection of orbital electrons) and excitation (raising electrons to higher energy levels within the atom).
2. The chemical phase — these damaged atoms and molecules react with other cellular components leading to the breakage of chemical bonds and the formation of 'free radicals'.
3. The biological phase — this includes all subsequent processes, beginning with enzymatic reactions that act on the residual chemical damage. The vast majority of DNA damage is repaired successfully but some lesions fail to repair and this leads to cell death. In most tissues, several cell divisions may occur prior to cell death.
4. The clinical phase — this covers the clinical effects of the delivered radiation. Tumour effects are thought to be generally due to cell death caused directly by DNA damage, although indirect effects such as reduction of tumour vascularity or enhanced immune recognition may also be important. Normal tissue effects may be *acute* due to direct cell death to mucosal surface or *late,* thought to be due to indirect effects on the vasculature or on the stem cell component, reducing the capacity to repair future damage. Radiation is also potentially carcinogenic and there is the risk of radiation-induced second malignancies, especially in younger patients and those expected to live a further 10 years.

The radiotherapy process

The process of RT is complex and involves an understanding of medical physics, radiobiology, radiation safety, dosimetry, radiation treatment planning, simulation and interaction of radiation with other treatment modalities. It consists of three distinct steps:

1. immobilization, imaging and target volume definition
2. treatment planning
3. treatment delivery and set up verification.

Immobilization, imaging and target volume definition

To ensure accurate delivery of radiotherapy over the several weeks of treatment, patients have to be appropriately immobilized (e.g.

Types of radiation treatment used

Type of radiation	Indication
Photons	Able to penetrate deep into the body while sparing the skin. Commonest modality used for most deep-seated tumour types, e.g. rectal cancer
Electrons	Provide a high dose to a few centimetres depth from the skin surface with little dose beyond. Therefore, used for superficial treatment, e.g. skin cancers
Protons	Deposit energy with extreme precision, therefore limiting unwanted dose. Currently used for paediatric cancers, skull base cancers and some spinal tumours
Brachytherapy	Radioactive sealed sources temporarily or permanently inserted into the tumour, e.g. cervical and prostate cancer
Injected radiotherapy	Radio-iodine for thyroid cancer and strontium-89 for bone metastases

Table 1

with the use of thermoplastic shells for head and neck cancers) and positioned on the treatment couch in such a way that the patient's position is comfortable, reproducible and optimal for the way the treatment will be delivered (e.g. supine and arms up for thoracic cancers). A planning CT scan is then performed in the treatment position and this is used to define the area to be treated. All diagnostic information available should be used to define the tumour and this will include clinical examination findings and diagnostic imaging or procedures (e.g. CT, MRI, PET, endoscopic ultrasound). Three volumes are usually drawn: the GTV (gross tumour volume) consists of the actual tumour that is then extended with a margin for microscopic spread to create the CTV (clinical target volume).[3] The CTV often also includes nodal areas at risk. A further margin is added to the CTV to allow for potential daily variation in tumour position, which can be from patient positioning or from internal organ motion. This is known as the PTV or planning target volume and ensures that the CTV is always treated.

Treatment planning

The next part of the process is to create a combination of RT beams that will deliver the dose required to the PTV (Figure 1). At this stage, critical normal structures surrounding the target volume are outlined, known as 'organs at risk' (OARs). These are structures that limit the dose that can be delivered to the target volume (e.g. the rectum is an OAR for prostate RT). Planning is done by the physicists using a combination of three or more beams entering from different directions. Physical avoidance of normal structures is important to minimize toxicity. Once a plan is created, it is approved by the clinician and the data is transferred to the treatment machine.

Treatment delivery and set up verification

Prior to each treatment, the patient must be set up in the same position as they were for the planning scan to ensure the radiation is delivered to the same place each day. Various forms of imaging techniques have been developed to verify the set up and to visualize

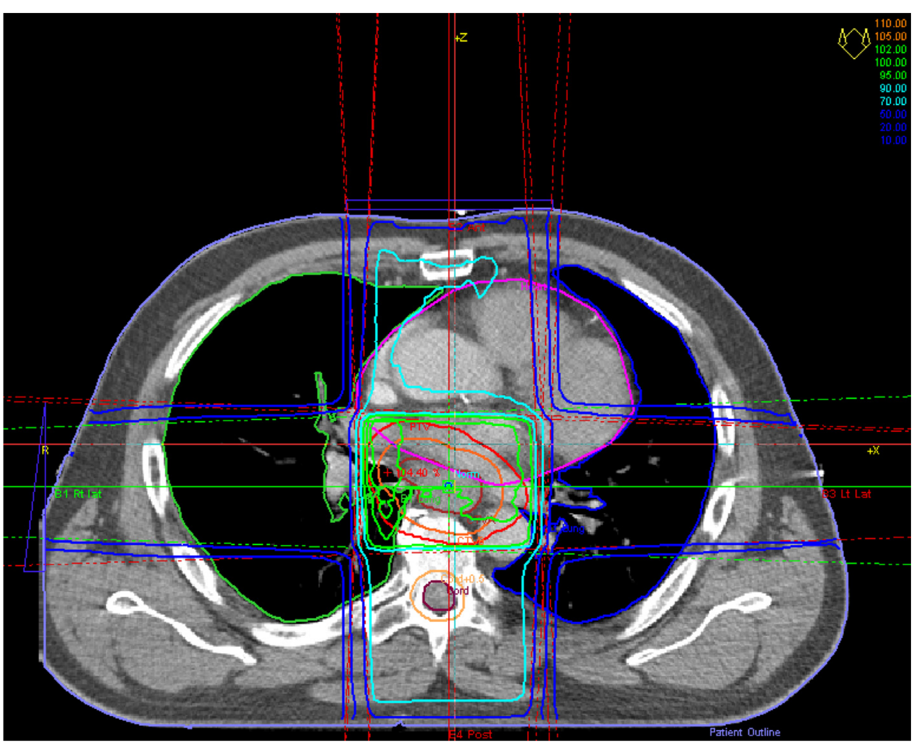

Figure 1 Three-dimensional conformal radiotherapy plan of an oesophagus showing four beams entering from the front and back and one from left and one from the right. The red outline (labelled PTV) is the volume to be treated and the coloured lines are the dose lines (isodoses) indicating what dose the structures contained within that line receive. The ideal plan would have all the PTV contained within the 95% isodose with no areas of high dose outside of this volume.

