

# Radiation physics and applications in therapeutic medicine

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## Abstract

Radiation therapy is an example of the successful application of advanced physics to the treatment of human disease leading to improved quality of life and even cure for many patients. The German physicist William Roentgen (1845–1923), who discovered x-rays in 1895 and pioneered early x-ray applications, would likely be astonished if he could see the breadth and depth of their application in the modern hospital setting. This article gives an overview of some modern applications of high energy radiation beams in therapeutic medicine and the underlying physics which forms the basis of their curative effects.

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## Radiation biology—what does radiation do to cancer cells?

Cancer cells are characterized by uninhibited and prolific replication which can interfere with the function of normal cells and organs, thereby endangering the life of the patient. The aim of radiation treatment is to deliver a sufficient radiation dose to sterilize cancer cells while limiting accidental damage to adjacent healthy tissue. But what is ‘dose’, and what does it mean to sterilize a cell? Radiation dose is the energy absorbed by cells from an incident radiation beam, per unit mass of tissue, and is a measure of molecular damage inflicted on the cells. Many different types of radiation have been investigated for cancer-cell killing efficacy with varying results: these include beams of photons, electrons, neutrons, protons, pions and even heavy atoms like carbon-12. The majority of modern clinics use photon and/or electron beams to treat cancer, and these beams disrupt normal cellular function principally by breaking chemical bonds through ionizing interactions. These ionizations can corrupt key molecules required

for cellular replication and metabolism. A cell is sterilized when sufficient molecular damage has been inflicted that the cell can no longer replicate. Note that while cancer cell-death may be preferable, cell sterilization is often sufficient to preserve the life of the patient.

Radiation damage to DNA molecules in the cell nucleus is the primary mechanism for cell sterilization. DNA contains coded instructions for the entire functionality of the cell, and when a cell replicates the DNA divides and an identical copy is made for the offspring cell. Radiation damage to DNA can prevent cell replication and the viability of the offspring cell. Radiation biologists have developed the linear–quadratic (LQ) mathematical model to describe radiation sterilization of cancer cells. The model assumes that a cell is sterilized when both strands of a DNA double helix molecule are broken. This can occur either by a single particle that breaks both strands at the same time, or by two particles that each break one of the strands with a short time interval between breakages. The significant difference between this ‘single’ or ‘double’ DNA hit is that normal cellular

repair mechanisms can repair some or all of the double hit damage (the first broken strand may be repaired before the second strand is broken) but these mechanisms are unable to repair the substantial damage when both strands are broken at the same time. According to the LQ model, the surviving fraction of cells  $S_{fx}$  after a dose of radiation  $D$  is given by

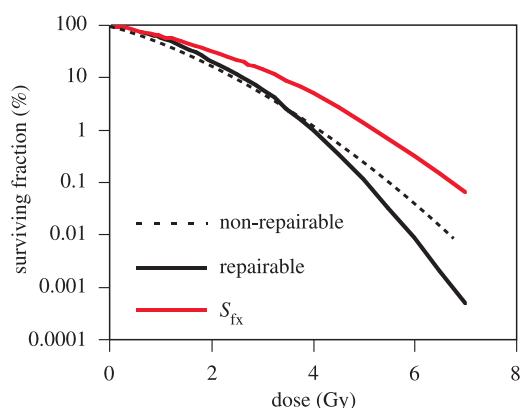
$$S_{fx} = \exp(-\alpha D - \beta D^2) \quad (1)$$

where  $\alpha$  is the coefficient of non-repairable damage and  $\beta$  is the coefficient of repairable damage. A plot of  $\log(S_{fx})$  against dose is called a cell-survival curve and an example is shown in figure 1.

Empirical tests determine that DNA repair mechanisms of tumour cells are significantly less effective than those of normal healthy cells (i.e. tumour cells exhibit low values of  $\beta$ ). This effect is exploited by ‘fractionating’ the radiation treatment into a succession of small doses, typically one dose-fraction a day for 6–7 weeks. After each fraction the normal healthy cells are able to repair some of the radiation damage whereas the tumour cells are unable to repair the damage, leading to compounded decimation with each new fraction. The fractionation is optimized when maximum cancer cell sterilization is achieved with minimal damage to normal tissues. Determining the optimal trade-offs between dose per fraction, time interval between fractions and total treatment dose is the subject of a great deal of current research.

### How do we generate radiation in a hospital setting?

Photon beams are used for both the localization and treatment of human tumours. Localization is the process of defining the physical extent and location of the tumour and is performed using low energy ‘diagnostic’ x-rays, typically 0.03 MeV mean energy, which yield relatively high soft-tissue/bone contrast. Low energy diagnostic beams are ineffective for therapy of most cancers, however, as they have poor penetration (especially through bone) and a significant fraction of radiation scatters out of the treatment region. Radiation therapy therefore utilizes high energy photon and electron beams, typically with a mean energy of 2–10 MeV. The problem of generating radiation therefore



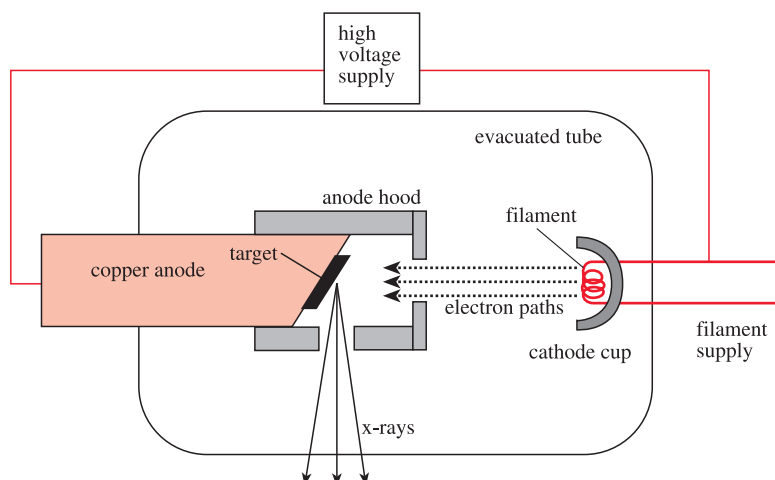
**Figure 1.** Cell survival curve illustrating the surviving fraction of cells after a single dose of radiation. The repairable and non-repairable components are also shown.

falls into two divisions: the production of low and high energy x-rays. Interestingly, although the two divisions differ dramatically in technical implementation, they both employ the same physical mechanism of radiation generation—the bremsstrahlung interaction.

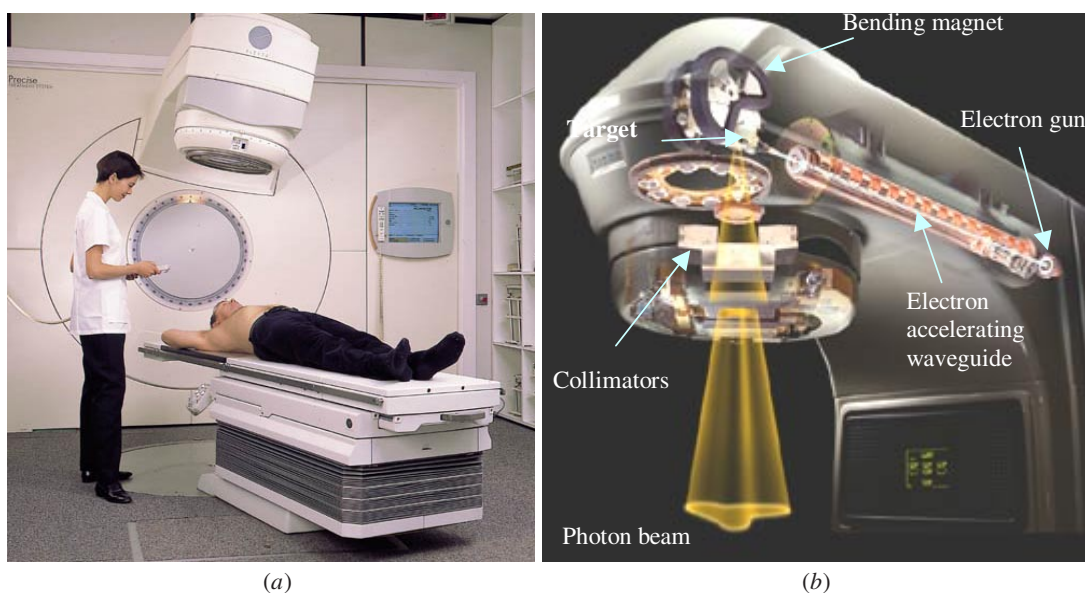
Bremsstrahlung, or braking radiation, is the phenomenon whereby a fast moving electron is suddenly decelerated by coulombic interaction with a heavy, positively charged target nucleus. During deceleration the electron radiates away some of its energy in the form of a photon. In general, faster moving electrons radiate a greater fraction of their energy as bremsstrahlung photons and deposit less heat to the heavy target atoms. In a low-energy x-ray generator (figure 2) electrons emitted from a heated filament via thermionic emission are accelerated across an evacuated tube to strike a high- $Z$  tungsten target where the bremsstrahlung interaction occurs. Notice how the radiation emerges almost at right angles to the direction of the incident electrons.

### *The Linear Accelerator: at the heart of radiation treatment!*

The low energy x-ray tube of figure 2 is only required to accelerate electrons to a few tenths of an MeV, which can be achieved with this simple design. Therapy machines are required to accelerate electrons up to 25 MeV, and this requires very high electromagnetic (EM) fields and a substantial number of high technology components. The Linear Accelerator is a



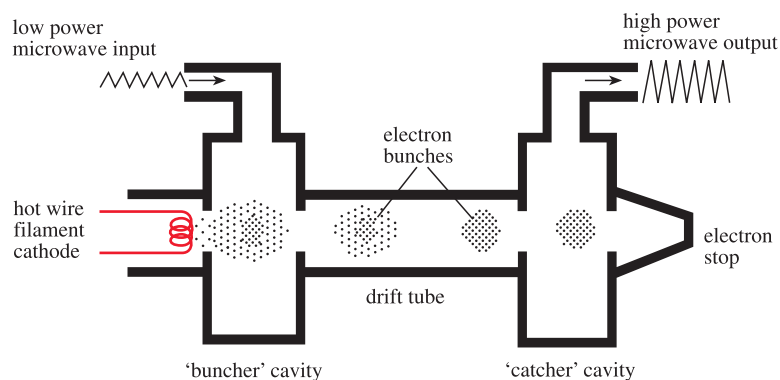
**Figure 2.** Low-energy diagnostic and superficial therapy x-ray tube.



**Figure 3.** The linear accelerator. (a) Treatment-room view of the Elekta travelling wave accelerator; (b) Schematic diagram of a standing wave accelerator.

technological wonder at the heart of the radiation therapy department, and generates both the high-energy photon and electron beams used in cancer therapy. It is usually located in a thick concrete underground bunker to minimize exposure to hospital staff and the general public. A treatment-room view and a schematic design are shown in figure 3. Echoes of the basic x-ray circuit are seen in the electron gun, corresponding to the filament, the main accelerator waveguide, where electrons are accelerated (necessarily longer than

in an x-ray tube) and the high-Z tungsten target. Intense EM fields generated by a complex resonant microwave cavity combination called a klystron accelerate electrons almost to the speed of light along the main waveguide of the accelerator. A variety of beam modifiers are placed in the beam to adapt it for clinical use. The most important modifiers are the flattening filter, which achieves a flat uniform beam, and the multi-leaf collimator, which shapes the cross section of the beam to match the projection of the tumour.



**Figure 4.** The klystron.

### *The klystron*

A cross-sectional drawing of an elementary two-cavity klystron is shown in figure 4. The klystron is able to massively amplify low-power input microwaves using two coupled resonant microwave cavities. Thermionic emission from a heated cathode introduces electrons into the first cavity, where they are 'bunched' together by the low-power input microwaves. The first cavity also exerts 'velocity modulation' on the electron bunches, which become progressively more distinct as they travel along the drift tube. The second resonant 'catcher' microwave cavity has intense electric fields induced on it by the electron bunches, which are consequently decelerated. Energy is thus transferred from the kinetic energy of the electron bunches to EM microwave power, which then exits the klystron and is transported to the main accelerator waveguide.

### **Treatment with photon beams**

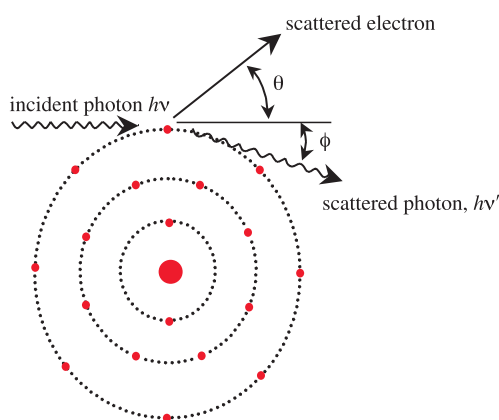
Photons are regarded as indirectly ionizing radiation. That is to say that photon interactions in tissue generate fast moving electrons that propagate through tissue directly damaging cells via multiple ionizations along the electron's track. Electron interactions are predominantly with orbital electrons of atoms and molecules in the tissue. Photons have greater penetrability into tissue than electrons (see figure 6) and therefore create significant electron fluence at depth, without giving excessive dose to the intervening healthy tissue. Although photons penetrate tissue quite well, they still deposit significant dose superficially. To maintain the

surface dose below acceptable levels several photon beams are generally used in crossfire techniques. All the beams in the treatment plan contribute dose to the tumour, at the point of crossfire, but surface tissue generally only receives dose from one or two beams.

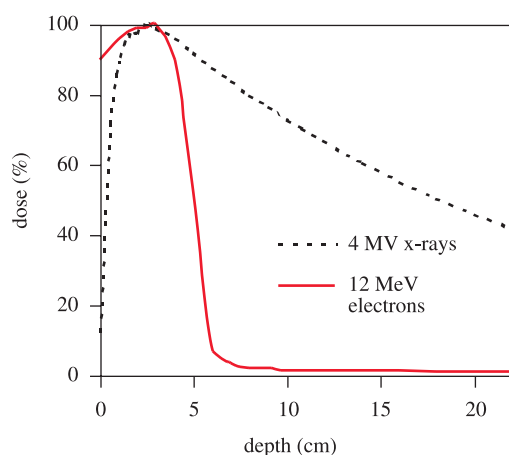
### *Physical interactions*

There are three main physical interaction mechanisms by which a therapeutic energy photon can interact with human tissue: the photoelectric effect, Compton scattering and pair production. The relative probabilities of each interaction are simple functions of the energy of the incident photon and the atomic mass number of the target atom. More complicated relations relate interaction probability to parameters like the scattering angle and energy distribution amongst particles. Over the therapeutic range of energies considered here, Compton scattering is generally the dominant mechanism, although photoelectric absorption becomes important at lower energies ( $< 100$  keV) and pair production becomes important at high energies ( $> 5$  MeV).

A schematic diagram of the Compton scattering interaction is shown in figure 5. An incident photon scatters off an outer orbital electron with reduced energy. The electron leaves the atom carrying off the energy difference between the incident and scattered photons. In the photoelectric effect, the incident photon interacts with an inner bound orbital electron. The incident photon is completely absorbed in the interaction (i.e. no scattered photon) and the electron leaves the atom carrying off the difference energy accounting for the binding energy of the electron



**Figure 5.** Schematic diagram of inelastic Compton scattering. An outer orbital ‘Compton’ electron is ejected from the atom by a high-energy incident photon, which loses energy in the interaction and is scattered.



**Figure 6.** Photon and electron depth-dose curves.

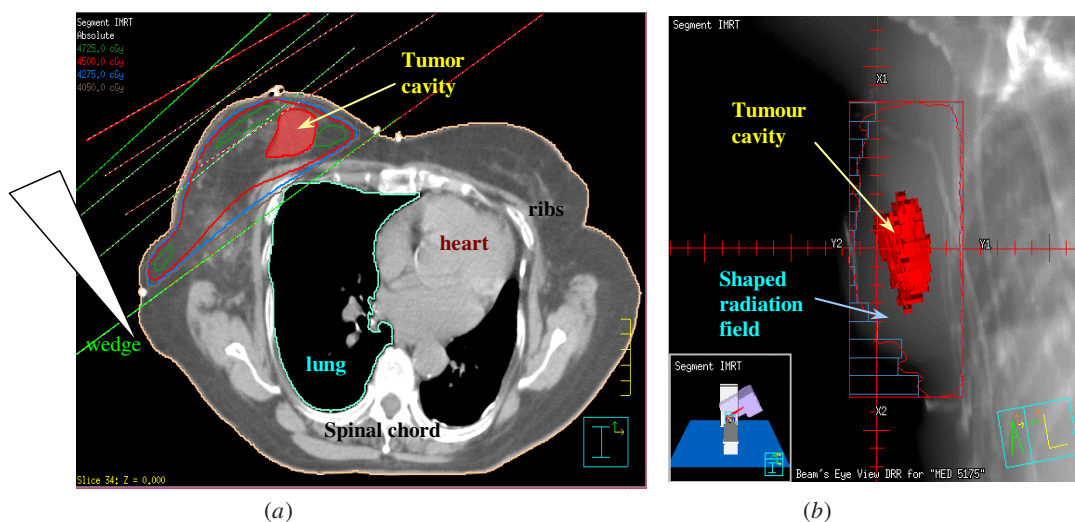
to the atom. In pair production, the incoming photon is once again completely absorbed, this time in an interaction with the field of the nucleus, resulting in the production of an electron-positron pair. The incident photon therefore has to have energy greater than the rest masses of the electron-positron pair. The positron causes ionization similar to an electron until it is brought to rest, when it annihilates with an electron producing a characteristic back-to-back 511 keV photon pair. A typical depth-dose curve for a clinical photon beam is illustrated in figure 6. A depth-dose curve for a typical electron beam is also shown to illustrate the increased penetration of the photon beam.

### *Clinical examples of photon beam treatment*

**Breast cancer.** Breast cancer is the most common malignant disease of women in the western world. The lifetime probability of a woman developing breast cancer is estimated to be about 11%. Breast cancer is a particularly dangerous disease because of its tendency to break through basement membranes of small tissue-ducts, leading to metastatic spread through the lymphatic system. Typical treatment will involve lumpectomy of the gross tumour followed by post-operative irradiation of the entire breast tissue. The entire breast is treated because of the microscopic invasive potential of breast cancer to the surrounding tissue to uniform dose.

A typical photon beam treatment arrangement and dose distribution are illustrated in figure 7. Two opposed tangential 6 MV radiation beams deliver a near-uniform dose to the breast and lumpectomy cavity. Dose uniformity is enhanced by placing metal wedge filters in the beam, which reduce the intensity of radiation progressively towards the thick end of the wedge. The wedge compensates for the ‘missing tissue’ towards the apex of the breast. Although both beams are wedged, only one is shown in figure 7. A typical radiation treatment course is a dose of 180 cGy per day, five days a week, to a total dose of 45 Gy. A boost dose to microscopic tumour residue around the surgical scar is sometimes given with an electron beam. Recent advances in breast radiotherapy (Kestin *et al* 2000) use intensity-modulated radiation therapy (IMRT), which leads to improved dose homogeneity and better cosmetic outcome.

**Prostate cancer.** Prostate cancer is the most common malignant disease of men in the US and Europe, with a lifetime probability of development of about 12%. Radiation therapy has been found to be as effective as radical prostatectomy for tumours limited to the prostate, and has considerably less toxicity. The prostate is located close to the rectum and bladder, and sophisticated treatment planning techniques are employed to shape the dose distribution to the shape of the prostate and to avoid excessive damage to these critical organs. An example of a four-field prostate treatment is shown in figure 8. The treatment plan consists of two pairs of beams: an anterior-posterior pair and a right-left lateral pair. The



**Figure 7.** (a) Transaxial view through a CT scan illustrating a typical radiation treatment for breast cancer. Two opposed wedged tangential 6 MV radiation beams (only one shown) deliver a near-uniform dose to the entire breast. Isodoses illustrate dose uniformity across the breast. (b) The radiation fields are shaped to minimize dose to lung and heart tissue.

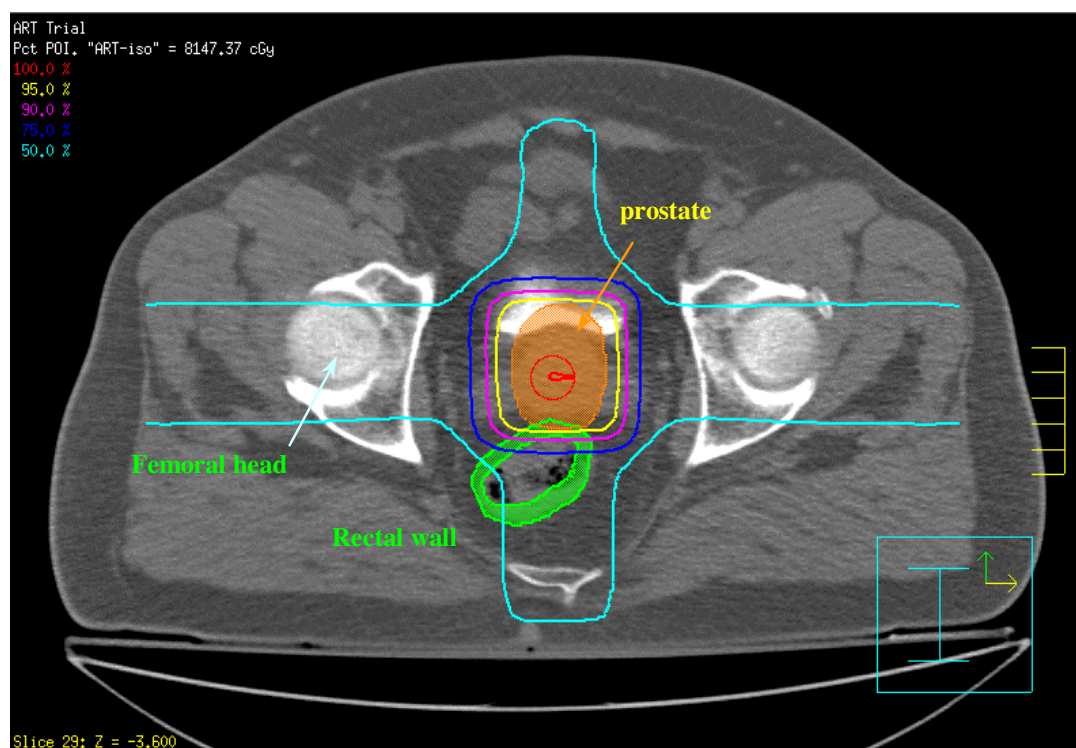
beams crossfire on the prostate to give a uniform therapeutic dose. Often higher energy photon beams ( $\geq 18$  MeV) are used to take advantage of their greater penetrability to the prostate, which can lie at depths of 18 cm or more. In a typical fractionated course of radiation therapy the patient will receive a daily dose of 180 cGy, five days a week, for eight weeks. Areas of current research interest include incorporating organ motion into treatment planning (Yan and Lockman 2001, Yan *et al* 2000), and online image-guided therapy, where anatomical information is obtained at the time of treatment (Jaffray and Siewerdsen 2000).

### Treatment with electron beams

Electron beams are obtained from the linear accelerator by simply moving the tungsten target out of the path of the accelerated electrons travelling along the waveguide of the accelerator. The electrons exit the head of the treatment machine and are incident on the patient after passing through a scattering foil which widens the beam and increases uniformity. Electron beams are useful for treating superficial lesions within 6 cm of the skin surface. The depth-dose curve illustrated in figure 6 shows that, unlike photons, the dose decreases rapidly with depth after a maximum value. Both the depth

of the maximum and the gradient of dose fall-off vary with the incident energy of the electrons. Electrons lose energy in tissue through coulombic interactions with atomic electrons and atomic nuclei (bremsstrahlung). In low- $Z$  materials (e.g. tissue) energy loss is predominantly by inelastic ionizing events with atomic electrons. The mean rate of energy loss of electrons in tissue is  $\sim 2$  MeV  $\text{cm}^{-1}$ . This means that a 10 MeV beam will have a maximum range of 5 cm. The dose distribution from electron beams can be difficult to predict, especially for small fields, due to electron scattering and build-up effects. Electrons ‘backscatter’ at an interface to a high- $Z$  material (e.g. metal dental implant or hip prosthesis), causing significant increase in dose upstream from the interface. In low-density regions like the lung, electrons can travel three times further than in normal tissue. In such cases it may be necessary to modify the angle of incidence of the treatment beam or the treatment dose to minimize the dose to healthy tissue.

A clinical example of the application of an electron beam would be to boost the dose to the surgical scar after lumpectomy of the breast. The surgical scar may be contaminated with sub-clinical tumour deposits during the surgical procedure. Electrons are also often used to boost the dose to superficial lymph nodes after a predetermined photon dose has been delivered.



**Figure 8.** Typical four-field radiation treatment for cancer of the prostate. Isodose lines show a uniform dose delivered to the whole prostate organ. The dose-limiting healthy structures are the rectum, bladder and femoral heads.

This ‘mixed-beam’ approach achieves dose at depth with the photon component with a boosted superficial dose from the electron component.

### What’s it like to have radiation treatment?

We have seen that a tremendous amount of activity occurs at the atomic and subatomic level when a patient is irradiated with a photon or an electron beam. The patient, however, does not feel anything at all at the time of treatment. All the millions of interactions that take place in tissue are completely undetectable to the human nervous system at the time of treatment. Patients only feel the effects of their radiation treatment when significant numbers of targeted cells have been sterilized and removed by the immune system. This time interval depends on many issues like cell-cycle time and the structure and sensitivity of the irradiated tissue. Patients undergoing palliative treatment, when the aim is to improve quality of life rather than to cure the patient, often receive pain relief within a few days. Negative symptoms from radiation

treatment normally occur after 2–3 weeks if at all. Side effects that may occur are red and tender patches of skin, mild nausea and vomiting for abdominal treatments, diarrhoea and rectal discomfort for pelvic irradiation.

### The medical physicist and the radiation oncology treatment team

The patient interacts with a highly trained team of specialists who form the radiation oncology team. The primary roles in the team are the physician who determines the nature of the treatment, the physicist who advises on technical aspects, the dosimetrist who formulates the computer treatment plan, the therapist who delivers the treatment to the patient and the nurse who is the primary care-giver.

The medical physicist makes critically important contributions at many stages of the treatment process. The physicist is responsible for correct functioning of all aspects of radiation equipment, and for the purchasing and clinical acceptance and commissioning of

all new equipment. Research physicists are responsible for analysing treatment efficacy and for developing and implementing improvements whether from technological advances or new possibilities in treatment technique. An example is gel-dosimetry, a new technique for obtaining high resolution 3D images of complex dose distributions either by MR imaging or by laser-based optical-CT scanning (Oldham *et al* 2001). This is often a very interesting and challenging task given the rapid development of computing and technical hardware and software. The physicist also plays a critical role as the department troubleshooter, available at immediate notice to solve problems as they arise at treatment time and during the treatment planning process. Such a role often demands quick thinking in a stressful situation. The role of the medical physicist is a challenging one and demands high professional standards. At the same time it can be an exciting and rewarding profession, which makes a real difference to the quality of life of patients treated in the Radiation Therapy department.

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