MasterClass

Topic: Particles Therapy

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1. **What is Radiotherapy?**

Radiation therapy is a type of cancer treatment, but nowadays with radiation therapy we can treat some other diseases (heart,...) that uses beams of intense energy to kill cancer cells. Radiation therapy most often uses X-rays, but protons or other types of energy can also be used.
The term "radiation therapy" most often refers to external beam radiation therapy. During this type of radiation, the high-energy beams come from a machine outside of your body that aims the beams at a precise point on your body. During a different type of radiation treatment called brachytherapy, radiation is placed inside your body.
Radiation therapy damages cells by destroying the genetic material that controls how cells grow and divide. While both healthy and cancerous cells are damaged by radiation therapy. The goal of radiation therapy is to destroy as few normal, healthy cells as possible. Normal cells can often repair much of the damage caused by radiation, and this is the reason why in tretmant planing we used fractional radiation. Fractional radiation means that whole big dose which is purpose divide into small value and that value will be delivered every day. On this way we cill cancer cells and allow normal cells to repair.
Cancer can be detected using diagnostic methods. Some of them are scanning with CT (Computed Tomography), PET (Positron Emission Tomography) or with MRI (Magnetic Resonance Imaging) machines or some combination of these machines popular as hybrid. After diagnostic procedures a patient goes into treatment planing steady and after that on implementation radiation treatment. Radiation treatment is made by a medical physicist in cooperation with a oncologist doctor.

2. **Radiation units and doses**

When radiation goes through any kind of matter particles and photons interact with atoms in the matter, so for radiotherapy the matter is our body. During passing, the radiation leaves energy because of collisions. The increase of energy in the body constitutes the dose.
In fact exist some types of doses:

- Absorbed dose
- Equivalent dose
- Effectiv dose

Absorbed dose is defined as the energy deposited by ionizing radiation per unit mass of material and is expressed in $\frac{J}{kg}$. This unit represents Gy-gray or $1\frac{J}{kg}$.
Equivalent dose is defined as the absorbed dose multiplied with the radiation weight factor.

$$H_T = D \times w_R, \tag{1}$$

where D is an absorbed dose, w_R is a radiation weight factor. The measurement unit for equivalent dose is Sievert (Sv). Definition of sievert is the same as for gray because w_R is quantity without dimension, but to distinguish it from absorbed dose it was introduced as new. The following table presents the value weight factor for different types of the radiation.

Radiation type	Radiation weight factor
X-rays	1
γ-zrake	1
Electrons and positrons	1
Neutrons	Energy dependence
Protons 2 MeV	2
α particles and heavy ions	20

Effective dose referred to dose which is received by the whole body, and we get it by summing the equivalent dose for the every organ multiplied with the organ's weight factor. The value for the weight factor is dependant from the organ's sensitivity. The most sensitive organs are eye lenses, ovaries and testicles.

$$E = \sum H_T \times w_T, \tag{2}$$

where E is the effective dose, H_T is the equivalent dose and w_T is the organ's weight factor.

3. **Radiation damage**

Different particles and photons with different energy behave in different ways in our body. Radiation with lower energy has a shorter penetration then high energy. Because of different types of interaction different radiation causes different damages in our cells. Radiation in a primary way affects DNA. Our DNA is consisted of two connected polynucleotide chains and formed into a helix shape.

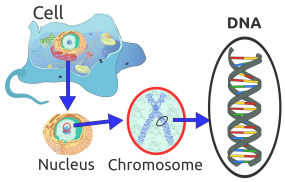


Figure 1

This chains are broken up by radiation, and after that normal cells can be fully repaired, incorrectly repaired or can die. The first situation is the best but isn't

always possible, then appears the second or third option. The second one is the most damaging because after it a mutation appears in the cells which may develop into a cancer later on. This is one of the reasons why heavy ions and protons are the future of radiotherapy, because these particles cause brake up in both chains and cause cellular death which does not allow the cells to mutate, this is different for photons because they cause the brake up one of the DNA chains and the probability of a mutation is bigger. On the other side cancer cells don't have a repair system and after damaging their DNA they die but in some case cancer is resistant to photon radiation, well this is one more reasons why we should use protons or carbon ions because protons and carbon ions have a bigger probability to destroy resistant cancer cells than photons.

3.1. **RBE (relative biological effectiveness)**

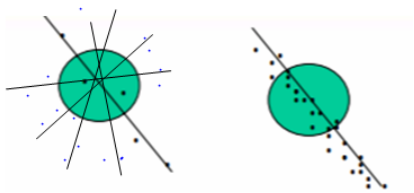


Figure 2

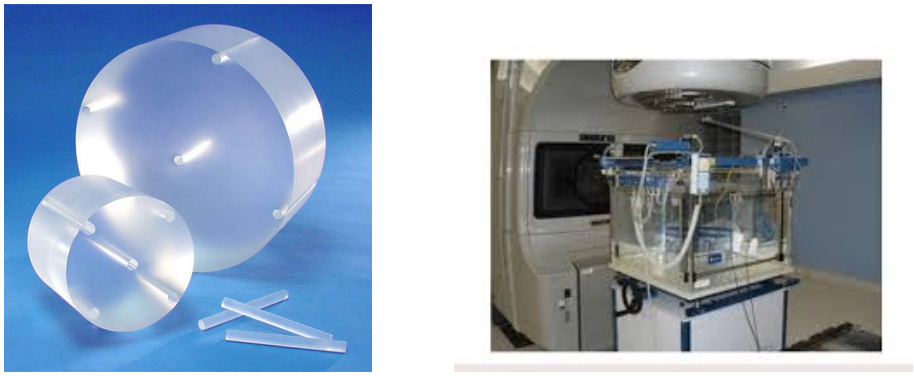
As we said different types of radiation deposit energy in biological tissues in different ways, which affects the amount of cellular damage. RBE (relative biological effectiveness) is a relative measure of the damage done by a given type of radiation per unit of energy deposited in biological tissues.The reference radiation (Dx) is usually 220 kVp x-ray or 60Co γ photons. The ratio is written as $RBE = \frac{Dx}{D}$. RBE is an important parameter for estimating the risk from exposure to ionizing radiation (IR). Compared with higher energy photons such as cobalt-60 gamma rays, lower energy electrons and photons produce more dense clusters of ionizations, leading to more complex damage to the cell's DNA, and thus a higher RBE.

Radiotherapy Tretmant Planing

Phantoms

Basic dose distribution data are usually measured in a water phantom, which closely approximates the radiation absorption and scattering properties of muscle and other soft tissues. Another reason for the choice of water as a phantom material is that it is universally available with reproducible radiation properties.Since it is not always possible to put radiation detectors in water, solid phantoms have been developed as substitutes for water. Ideally, for a given material to be tissue or water equivalent, it must have the same effective atomic number, number of electrons per gram, and mass density. However, since the Compton effect is the most predominant mode of interaction for megavoltage photon beams in the clinical range, the necessary condition for water equiva-

lence for such beams is to have the same electron density (number of electrons per cubic centimeter) as that of water.



(a) (b)

Figure 3: Phantoms

Depth Dose Distribution

As the beam is incident on a patient (or a phantom), the absorbed dose in the patient varies with depth. This variation depends on many conditions: beam energy, depth, field size, distance from source, and beam collimation system. Thus, the calculation of dose in a patient involves considerations in regard to these parameters and others as they affect depth dose distribution. An essential step in the dose calculation system is to establish depth dose variation along the central axis of the beam. In phantoms depth dose distribution can be measured with different types of detectors(chambers, semiconductor detectors, TLD (thermoluminescent dosimeters)). Different kindes of beam has different depth dose distribution.

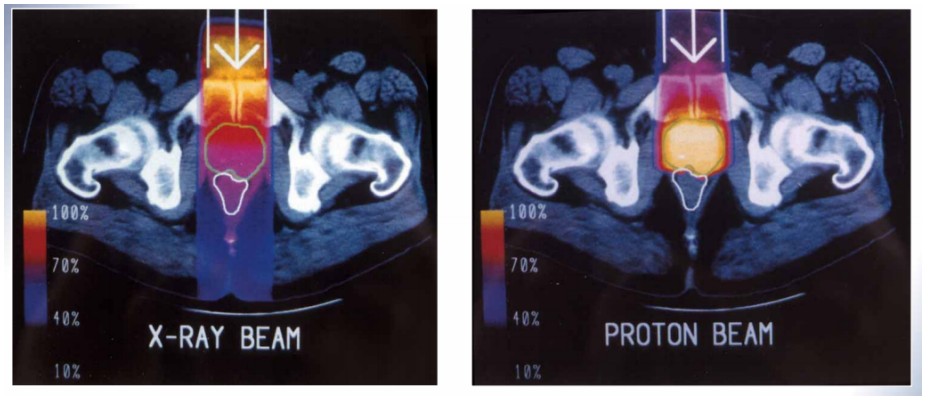
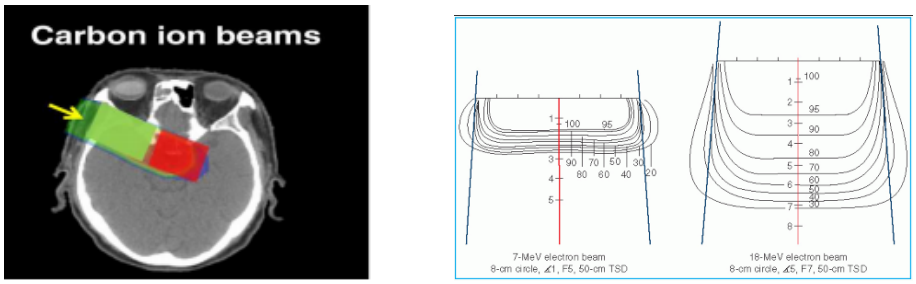


Figure 4



(a) (b)

Figure 5

An isodose chart for a given beam consists of a family of isodose curves usually drawn at equal increments of percent depth dose, representing the variation in dose as a function of depth and transverse distance from the central axis. The depth dose values of the curves are normalized either at the reference point of maximum dose on the central axis.
Field size may be specified either geometrically or dosimetrically. The *geometric field* size is defined as "the projection, on a plane perpendicular to the beam axis, of the distal end of the collimator as seen from the front center of the source. This definition usually corresponds to the field defined by the light localizer, arranged as if a point source of light were located at the center of the front surface of the radiation source. The dosimetric, or the physical, field size is the distance intercepted by a given isodose curve (usually 50% isodose) on a plane perpendicular to the beam axis at a stated distance from the source. Unless stated otherwise, the term field size will denote geometric field size. In addition, the field size will be defined at a predetermined distance such as SSD or the source to axis distance (SAD). The latter term is the distance from the source to axis of gantry rotation known as the isocenter.

Multiple Fields

One of the most important objectives of treatment planning is to deliver maximum dose to the tumor and minimum dose to the surrounding tissues this proces called optimizations. In addition, dose uniformity within the tumor volume and sparing of critical organs are important considerations in judging a plan. Some of the strategies useful in achieving these goals are (a) using fields of appropriate size, (b) increasing the number of fields or portals, (c) selecting appropriate beam directions, (d) adjusting beam weights (dose contribution from individual fields), (e) using appropriate beam energy, and (f) using beam modifiers such as wedge filters and compensators. Although obtaining a combination of these parameters that yields an optimal plan is time consuming if done manually, treatment-planning computers are now available that can do the job quickly and accurately. These systems are highly interactive so that the user

can almost instantly modify, calculate, and examine various plans to select one that is clinically superior.

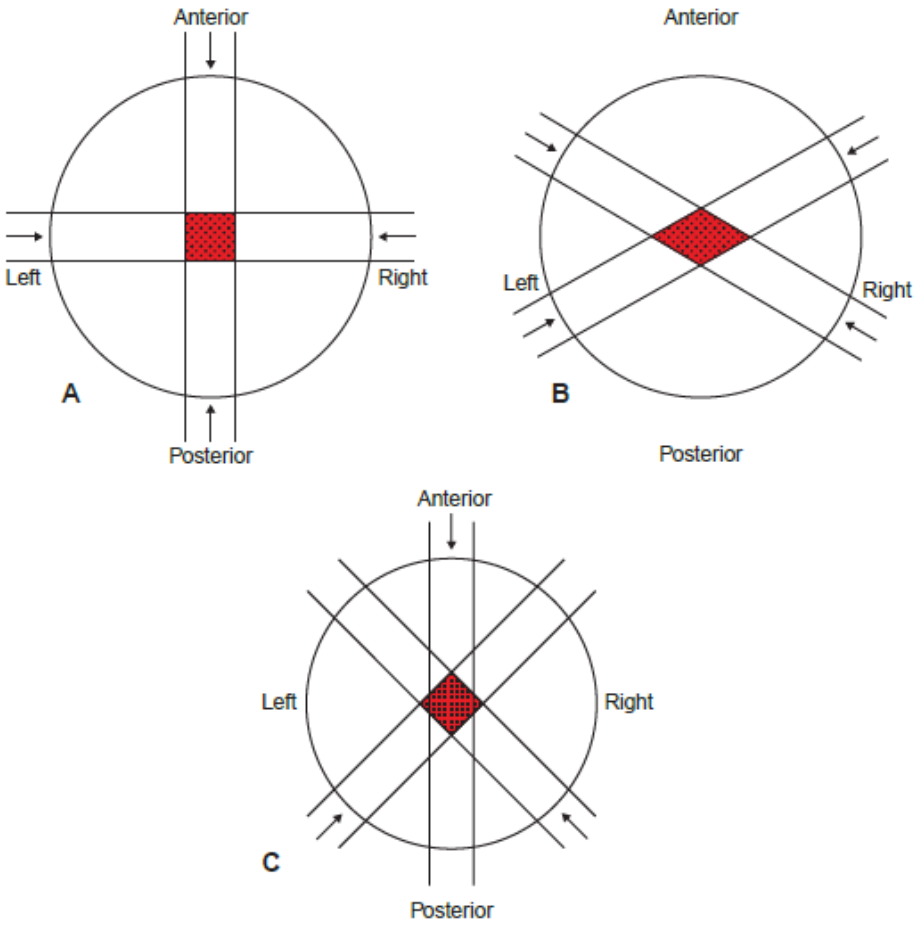


Figure 6

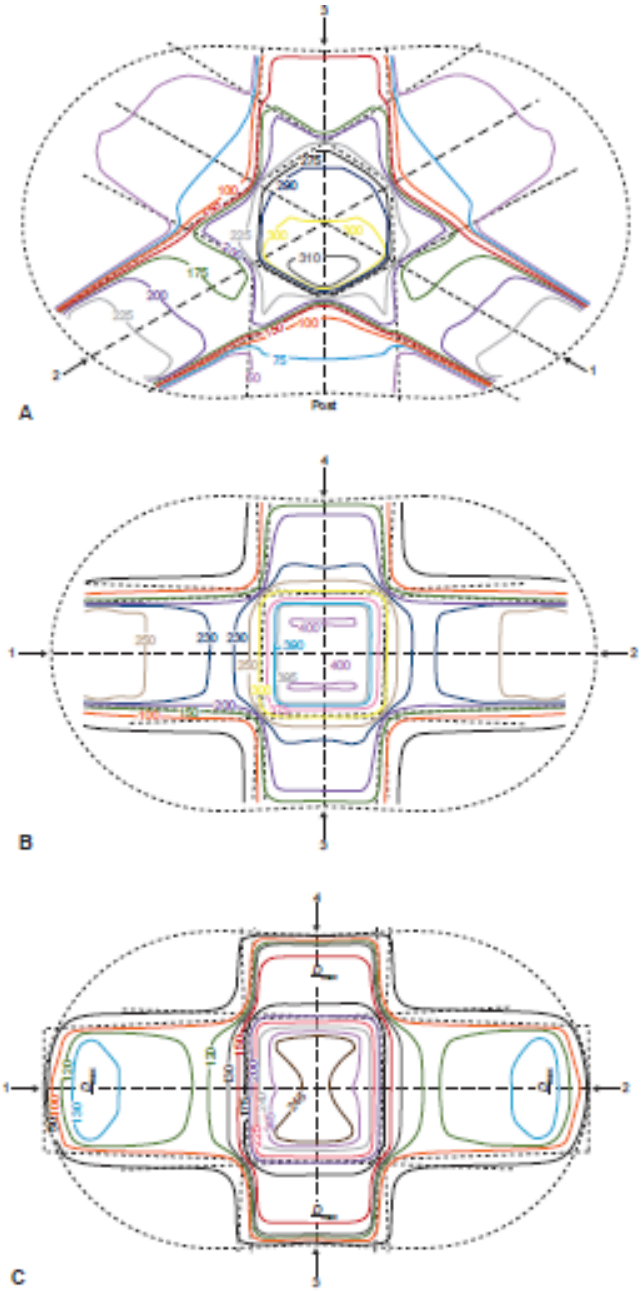


Figure 7: Examples of multiple field plans. A: Three-field B: Four-field C: Four-field

STATIONARY BEAMS

The isocentric technique of irradiation consists of placing the isocenter of the machine at a depth within the patient and directing the beams from different directions. The distance of the source from the isocenter, or the SAD, remains constant irrespective of the beam direction.

ROTATION THERAPY

Rotation therapy is a special case of the isocentric technique in which the beam moves continuously about the patient, or the patient is rotated while the beam is held fixed. Although this technique has been used for treating tumors of the esophagus, bladder, prostate gland, cervix, and brain, the technique offers little advantage over the isocentric technique using multiple stationary beams. For example, the esophagus can be treated equally well with three fields; the prostate gland and bladder, with four fields (sometimes combined with parallel opposed fields); and the brain, with two or three fields

ICRU Volumes (International Commission on Radiation Units and Measurements)

Gross Tumor Volume

The gross tumor volume (GTV) is the gross demonstrable extent and location of the tumor. It may consist of primary tumor, metastatic lymphadenopathy, or other metastases. Delineation of GTV is possible if the tumor is visible, palpable, or demonstrable through imaging. GTV cannot be defined if the tumor has been surgically removed, although an outline of the tumor bed may be substituted by examining preoperative and postoperative images.

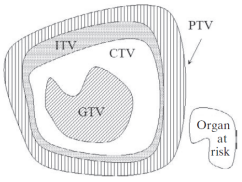


Figure 8

Clinical Target Volume

The clinical target volume (CTV) consists of the demonstrated tumor(s) if present and any other tissue with presumed tumor. It represents therefore the true extent and location of the tumor. Delineation of CTV assumes that there are no tumor cells outside this volume. The CTV must receive adequate dose to achieve the therapeutic aim.

Internal Target Volume

ICRU Report 62 (15) recommends that an internal margin (IM) be added to CTV to compensate for internal physiologic movements and variation in size, shape, and position of the CTV duringtherapy in relation to an internal reference point and its corresponding coordinate system. The volume that includes CTV with these margins is called the internal target volume (ITV).

Planning Target Volume

The volume that includes CTV with an IM as well as a setup margin (SM) for patient movement and setup uncertainties is called the planning target volume (PTV). To delineate the PTV, the IM and SM are not added linearly but are combined rather subjectively. The margin around CTV in any direction must be large enough to compensate for internal movements as well as patient motion and setup uncertainties.

Planning Organ at Risk Volume

The organ(s) at risk (OR) needs adequate protection just as CTV needs adequate treatment. Once the OR is identified, margins need to be added to compensate for its movements, internal as well as setup. Thus, in analogy to the PTV, one needs to outline planning organ at risk volume (PRV) to protect OR effectively. Figure schematically illustrates the process of outlining PTV and PRV. This process is intended to make the radiation oncologist think methodically and analytically when outlining targets and organs at risk. Although absolute accuracy in either case cannot be assured, the objective of this approach is to minimize errors by paying attention to details.It is also important to point out that there is a common tendency among practitioners to draw target volumes based on GTV with little margins to account for subclinical disease, organ motion, or setup uncertainties. The so-called conformal radiation therapy is a double-edged sword—a high degree of plan conformity can create a high probability of geographical miss. Thus, great caution must be exercised in designing PTV and PRV. It is just as important to know the limitations of the system as it is to know its capabilities.

Treated Volume

Additional margins must be provided around the target volume to allow for limitations of the treatment technique. Thus, the minimum target dose should be represented by an isodose surface that adequately covers the PTV to provide that margin. The volume enclosed by this isodose surface is called the treated volume. The treated volume is, in general, larger than the planning target volume and depends on a particular treatment technique.

~~Irradiated Volume~~

~~The volume of tissue receiving a significant dose (e.g., 50% of the specified target dose) is called the irradiated volume. The irradiated volume is larger than the treated volume and depends on the treatment technique used.~~

~~Maximum Target Dose~~

~~The highest dose in the target area is called the maximum target dose, provided this dose covers a minimum area of 2 cm2. Higher dose areas of less than 2 cm2 may be ignored in designating the value of maximum target dose.~~

~~Minimum Target Dose~~

~~The minimum target dose is the lowest absorbed dose in the target area.~~

~~Mean Target Dose~~

~~If the dose is calculated at a large number of discrete points uniformly distributed in the target area, the mean target dose is the mean of the absorbed dose values at these points.~~

Median Target Dose

The median target dose is simply the value between the maximum and the minimum absorbed dose values within the target.

Modal Target Dose

The modal target dose is the absorbed dose that occurs most frequently within the target area. If the dose distribution over a grid of points covering the target area is plotted as a frequency histograph, the dose value showing the highest frequency is called the modal dose.

Hot Spots

A hot spot is an area outside the target that receives a higher dose than the specified target dose. Like the maximum target dose, a hot spot is considered clinically meaningful only if it covers an area of at least 2 cm2.

Data Acquisition

Acquisition of body contours and internal structures is best accomplished by 3-D volumetric imaging [computed tomography (CT), magnetic resonance imaging (MRI), etc.]. The scans are performed specifically for treatment-planning purposes, with the patient positioned the same way as for actual treatment. In 3-D treatment planning (Chapter 19), these data are all image based and are

acquired as part of the treatment-planning process. However, for cases in which 3-D treatment planning is not considered necessary or if body contours are obtained manually for verification of the image-based contours, mechanical or electromechanical methods are used for contouring.

Computed Tomography

In CT, a narrow beam of x-rays scans across a patient in synchrony with a radiation detector on the opposite side of the patient. If a sufficient number of transmission measurements are taken at different orientations of the x-ray source and detector (Fig. 12.2A), the distribution of attenuation coefficients within the layer may be determined. By assigning different levels to different attenuation coefficients, an image can be reconstructed that represents various structures with different attenuation properties.

Magnetic Resonance Imaging

MRI has developed, in parallel to CT, into a powerful imaging modality. Like CT, it provides anatomic images in multiple planes. Whereas CT provides basically transverse axial images (which can be further processed to reconstruct images in other planes or in three dimensions), MRI can be used to scan directly in axial, sagittal, coronal, or oblique planes. This makes it possible to obtain optimal views to enhance diagnostic interpretation or target delineation for radiotherapy. Other advantages over CT include not involving the use of ionizing radiation, higher contrast, and better imaging of soft tissue tumors. Some disadvantages compared with CT include lower spatial resolution.

Positron emission tomography

Positron emission tomography (PET) provides functional images that can, in some cases, differentiate between malignant tumors and the surrounding normal tissues. This capability can be combined with the anatomic information provided by a CT scanner to complement each other.The idea of combining both of these modalities into a single system for simulation has led to the development of PET/CT.

Patient treatment position and immobilization devices

Depending on the patient treatment position or the precision required for beam delivery, patients may or may not require an external immobilization device for their treatment. Immobilization devices have two fundamental roles:

- To immobilize the patient during treatment
- To provide a reliable means of reproducing the patient's position from simulation to treatment, and from one treatment to another

The simplest immobilization means include masking tape, Velcro belts or elastic bands. The basic immobilization device used in radiotherapy is the head rest, shaped to fit snugly under the patient's head and neck area, allowing the patient to lie comfortably on the treatment table. Modern radiotherapy generally requires additional immobilization accessories during the treatment of patients. Patients to be treated in the head and neck or brain areas are usually immobilized with a plastic mask that, when heated, can be moulded to the patient's contour. The mask is affixed directly on to the treatment table or to a plastic plate that lies under the patient, thereby preventing movement. For treatments to the thoracic or pelvic area, a variety of immobilization devices are available. Vacuum based devices are popular because of their reusability. Basically, a pillow filled with tiny Styrofoam balls is placed around the treatment area and a vacuum pump evacuates the pillow, leaving the patient's form as an imprint on the pillow. The result is that the patient can be positioned snugly and precisely on the pillow prior to every treatment. Another system, similar in concept, uses a chemical reaction between reagents in the pillow to form a rigid mould of the patient. Special techniques, such as stereotactic radiosurgery, require such high precision that conventional immobilization techniques are inadequate.

Figure 9

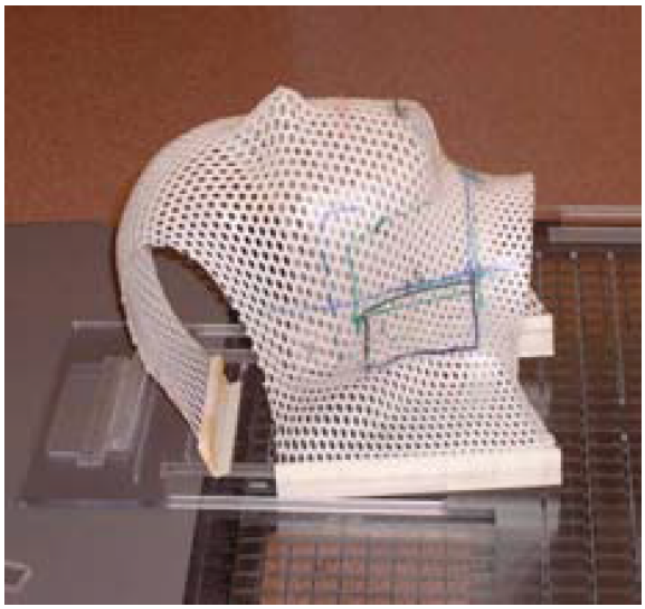


Figure 10

Modern Radiation Therapy

Three-Dimensional Conformal Radiation Therapy

By three-dimensional conformal radiotherapy (3-D CRT), we mean treatments that are based on 3-D anatomic information and use treatment fields that conform as closely as possible to the target volume in order to deliver adequate dose to the tumor and minimum possible dose to normal tissue. The concept of conformal dose distribution has also been extended to include clinical objectives such as maximizing tumor control probability (TCP) and minimizing normal tissue complication probability (NTCP). Thus, the 3-D CRT technique encompasses both the physical and biologic rationales in achieving the desired clinical results.

Dose Volume Histograms

Display of dose distribution in the form of isodose curves or surfaces is useful because it shows not only regions of uniform dose, high dose, or low dose, but also their anatomic location and extent. In 3-D treatment planning, this information is essential but should be supplemented by DVHs for the segmented structures, for example, targets and critical structures. A DVH not only provides quantitative information with regard to how much dose is absorbed in how much volume, but also summarizes the entire dose distribution into a single curve for each anatomic structure of interest. It is, therefore, a great tool for evaluating

a given plan or comparing competing plans.
The DVH may be represented in two forms: the cumulative integral DVH and the differential DVH. The cumulative DVH is a plot of the volume of a given structure receiving a certain dose or higher as a function of dose (Fig. 19.6). Any point on the cumulative DVH curve shows the volume that receives the indicated dose or higher. The differential DVH is a plot of volume receiving a dose within a specified dose interval (or dose bin) as a function of dose.

Intensity-Modulated Radiation Therapy

The term intensity-modulated radiation therapy (IMRT) refers to a radiation therapy technique in which a nonuniform fluence is delivered to the patient from any given position of the treatment beam to optimize the composite dose distribution. The treatment criteria for plan optimization are specified by the planner and the optimal fluence profiles for a given set of beam directions are determined through "inverse planning." The fluence files thus generated are electronically transmitted to the linear accelerator, which is computer controlled, that is, equipped with the required software and hardware to deliver the intensity-modulated beams (IMBs) as calculated.
The clinical implementation of IMRT requires at least two systems: (a) a treatment-planning computer system that can calculate nonuniform fluence maps for multiple beams directed from different directions to maximize dose to the target volume while minimizing dose to the critical normal structures, and (b) a system of delivering the nonuniform fluences as planned. Each of these systems must be appropriately tested and commissioned before actual clinical use.

Stereotactic Radiotherapy and Radiosurgery

Stereotactic radiosurgery (SRS) is a single-fraction radiation therapy procedure for treating intracranial lesions using a combination of a stereotactic apparatus and narrow multiple beams delivered through noncoplanar isocentric arcs. The same procedure when used for delivering multiple dose fractions is called stereotactic radiotherapy (SRT). Both techniques involve threedimensional imaging to localize the lesion and delivering treatment that concentrates the dose in the target volume and spares as much as possible the normal brain.

Image-Guided Radiation Therapy

Image-guided radiation therapy (IGRT) may be defined as a radiation therapy procedure that uses image guidance at various stages of its process: patient data acquisition, treatment planning, treatment simulation, patient setup, and target localization before and during treatment. In the present context, we will use the term IGRT to signify radiotherapy that uses image guidance procedures for target localization before and during treatment.

Proton Beam Therapy

Basic principles of radiotherapy treatment planning for protons are essentially the same as for photons and electrons. These include acquisition of three-dimensional imaging data set, delineation of target volumes and organs at risk, setting up of one or more beams, selection of beam angles and energies, design of field apertures, optimization of treatment parameters through iterative or inverse planning, display of isodose distributions and dose volume histograms (DVHs), and so on, depending on the complexity of a given case.