Chapter 15

SPECIAL PROCEDURES AND TECHNIQUES IN RADIOTHERAPY

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15.1. INTRODUCTION

In addition to the routine conventional radiotherapy techniques used in standard radiotherapy departments and clinics, several specialized techniques are known and used for special procedures, be it in dose delivery or target localization. These techniques deal with specific problems that usually require equipment modifications, special quality assurance procedures and heavy involvement and support from clinical physicists. Owing to their increased complexity, these specialized techniques are usually available only in larger, regional centres.

The radiotherapy techniques that currently fall into the specialized category are listed below; the first six are special dose delivery techniques, the last three are special target localization techniques:

- Stereotactic irradiation;
- Total body irradiation (TBI) with photon beams;
- Total skin electron irradiation (TSEI);
- Intraoperative radiotherapy (IORT);
- Endorectal irradiation;
- Conformal radiotherapy and intensity modulated radiotherapy (IMRT);
- Image guided radiotherapy (IGRT);
- Respiratory gated radiotherapy;

- Positron emission tomography (PET)/computed tomography (CT) fused images.

15.2. STEREOTACTIC IRRADIATION

From an obscure irradiation technique practised in the 1960s and 1970s in only a few specialized centres, stereotactic irradiation has during the past 15 years developed into a mainstream radiotherapeutic technique practised in most major radiotherapy centres around the world. Stereotactic irradiation is the term used to describe focal irradiation techniques that use multiple non-coplanar photon radiation beams and deliver a prescribed dose of ionizing radiation to preselected and stereotactically localized lesions, primarily in the brain, although attempts have been made to extend the technique to other parts of the body.

The main characteristics of stereotactic irradiation are as follows:

- Total prescribed doses are of the order of 10–50 Gy, and the planning targets are small, with typical volumes ranging from 1 to 35 cm^3.
- The requirements for positional and numerical accuracy in dose delivery are ±1 mm and ±5%, respectively.
- The dose in stereotactic irradiation may be delivered through a stereotactic implantation of radioactive sources (stereotactic brachytherapy) or, more commonly, with one or several external radiation sources (stereotactic external beam irradiation).
- With regard to dose fractionation, stereotactic external beam irradiation (SEBI) is divided into two categories:
  - Stereotactic radiosurgery: the total dose is delivered in a single session.
  - Stereotactic radiotherapy: like in standard radiotherapy, the total dose is delivered in multiple fractions.
- From a technical point of view there is essentially no difference between stereotactic radiosurgery and stereotactic radiotherapy, and often the term radiosurgery is used to describe both techniques.
- Essentially any radiation beam that has been found useful for external beam radiotherapy has also found use in radiosurgery (cobalt γ rays, megavoltage X rays, proton and heavy charged particle beams, and even neutron beams).

15.2.1. Physical and clinical requirements for radiosurgery

The physical and clinical requirements for radiosurgery are as follows:

- Accurate determination of the target volume and its location with stereotactic techniques;
- Calculation of 3-D dose distributions inside and outside the target volume;
- Calculation of dose–volume histograms (DVHs) for the target and specific sensitive organs;
- Dose distributions that conform to target shapes and give a sharp dose fall-off outside the target volume;
- Direct superposition of isodose distributions on diagnostic images, showing the anatomical location of the target and surrounding structures;
- Accurate knowledge of the total dose and fractionation scheme required for treatment of the particular disease;
- Accurate positional (within ±1 mm) delivery of dose to the predetermined target;
- Accurate numerical (within ±5%) delivery of dose to the predetermined target;
- Dose delivery accomplished within a reasonable amount of time;
- Low skin dose (to avoid epilation) and low eye lens dose (to avoid cataracts);
- Low or negligible scatter and leakage dose to radiosensitive organs (to avoid subsequent somatic and genetic effects of radiation).

15.2.2. Diseases treated with stereotactic irradiation

The diseases treated with stereotactic irradiation are:

- Functional disorders;
- Vascular lesions;
- Primary benign and malignant tumours;
- Metastatic tumours.

15.2.3. Equipment used for stereotactic radiosurgery

The following equipment is used for stereotactic radiosurgery:

- A stereotactic frame, which defines a fixed coordinate system for an accurate localization and irradiation of the planning target volume (PTV). The stereotactic frame is also used for patient set-up on the treatment machine and for patient immobilization during the actual treatment procedure.

- Imaging equipment (CT, magnetic resonance (MR) and digital subtraction angiography (DSA)) with which the structures, lesions and PTVs are visualized, defined and localized.
- Target localization software, which is used in conjunction with the stereotactic frame system and imaging equipment to determine the coordinates of the target in the stereotactic frame reference system.
- A treatment planning system (TPS) with which the 3-D dose distribution for the radiosurgical treatment is calculated and superimposed on to the patient's anatomical information.
- An appropriate radiation source and radiosurgical treatment technique.

15.2.4. Historical development

The combined use of stereotaxy and irradiation in the treatment of disease was introduced in the early 1950s by the Swedish neurosurgeon Leksell, who also coined the term 'radiosurgery' to describe the technique. Leksell initially used 200 kVp X rays to deliver, in a single session, a high radiation dose (of the order of 100 Gy) to an intracranial target. He approached the target from several directions to focus the dose on the target within the brain and spare the surrounding vital structures.

Radiosurgery based on orthovoltage X rays was discontinued in the late 1950s but the idea of focal brain irradiation was carried over to other, more suitable, radiation beams, first to protons from cyclotrons, then to focused ^{60}Co γ rays and more recently to megavoltage X rays from linacs.

Linacs were proposed as viable radiation sources for radiosurgery in 1974 by Larsson. In 1984 Betti and Derechinsky reported on the development and clinical application of the linac based multiple non-coplanar arcs technique. Soon thereafter, the technique was introduced clinically in Vicenza (Italy) by Colombo and colleagues and in Heidelberg (Germany) by Hartmann and colleagues.

In 1986, Harvard University in Boston and McGill University in Montreal were the first two institutions to use linac based radiosurgery in North America. Harvard adopted the multiple non-converging arcs technique, while McGill developed its own radiosurgical technique, referred to as dynamic stereotactic radiosurgery.

15.2.5. Radiosurgical techniques

15.2.5.1. Gamma Knife

The Gamma Knife (also referred to as the gamma unit) is a radiosurgical device that has been associated with, and dedicated to, radiosurgery for the past four decades. Despite great technological advances during this time, the fundamental design and principles of the gamma unit have not changed much since Leksell introduced the prototype gamma unit in the late 1960s. The unit incorporates 201 ^{60}Co sources housed in the central body of the unit. These sources produce 201 collimated beams directed to a single focal point at a source to focus distance of about 40 cm. The final definition of the circular beam field size is provided by one of four helmets delivering circular fields with nominal diameters between 4 and 18 mm at the machine focal point. The main components of the gamma unit are:

- A radiation unit with an upper hemispherical shield and a central body;
- An operating table and sliding cradle;
- A set of four collimator helmets providing circular beams with diameters of 4, 8, 14 and 18 mm at the isocentre;
- A control unit.

A typical Gamma Knife installation depicting the main body of the machine, the treatment table and a collimator helmet is shown in Fig. 15.1.

15.2.5.2. Linac based radiosurgery

Linac based radiosurgery uses a standard isocentric linac with tight mechanical and electrical tolerances, modified for radiosurgery. The modifications are relatively simple and consist of:

— Supplementary collimation either in the form of a set of collimators to define small diameter circular radiosurgical beams or a micro multileaf collimator (MLC) to define small area irregular fields;
— A remotely controlled motorized table or treatment chair rotation;
— Table brackets or a floor stand for immobilizing the stereotactic frame during treatment;
— Interlocked readouts for angular and height position of the table;

FIG. 15.1. State of the art Gamma Knife (Model 4C) showing the main body of the unit containing 201 ^{60}Co sources (each nominally with an activity of 30 Ci = 1.11 × 10^{12} Bq), the treatment table and a collimator helmet deployed for treatment. The inset shows an up-close image of the automatic positioning system used to position the patient for treatment. (Courtesy of Elekta AB.)

— Special brakes to immobilize the vertical, longitudinal and lateral table motions during treatment.

Isocentric linac based radiosurgical techniques currently fall into three categories: multiple non-coplanar converging arcs, dynamic stereotactic radiosurgery and conical rotation. Each technique is characterized by a particular set of individual rotational motions of the linac gantry and the patient support assembly (table or chair) from given start to stop angles.

In the multiple non-coplanar converging arcs technique the patient is stationary either on the treatment table or chair while the gantry moves through a given arc. In the dynamic stereotactic radiosurgery technique both the gantry and the patient rotate simultaneously during the dose delivery (gantry 300º from 30º to 330º and table 150º from 75º to –75º). Figure 15.2 shows a patient being treated with the dynamic stereotactic radiosurgery technique.

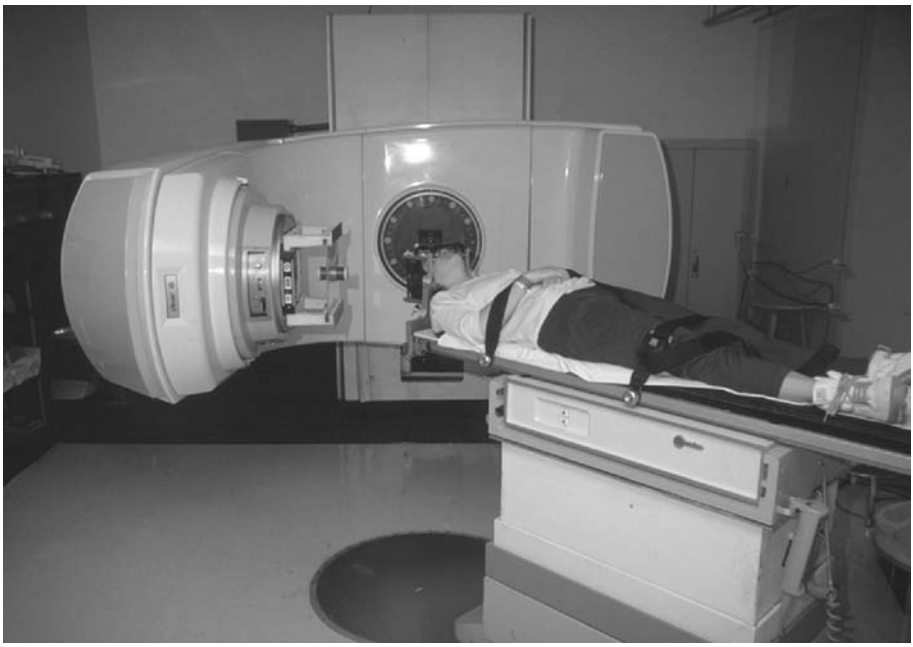

FIG. 15.2. Patient being treated with the dynamic stereotactic radiosurgery technique.

In conical rotation the patient rotates on a treatment chair while the gantry is stationary during the dose delivery. Of the three approaches, the multiple converging arcs technique is the most common, followed by dynamic rotation.

15.2.5.3. Miniature linac on robotic arm

A miniature linac on a robotic arm (CyberKnife) provides a radically new approach to linac based radiosurgery, both in target localization and in beam delivery. Instead of the conventional frame based stereotaxy, the system uses non-invasive image guided target localization, and instead of a conventional isocentric linac, the system uses a miniature 6 MV linac, operated in the X band at 10^4 MHz and mounted on an industrial robotic manipulator. A typical installation of a robotic arm mounted linac is shown in Fig. 15.3.

The CyberKnife stereotactic radiosurgery system broadens the range of traditional stereotactic radiosurgery and offers the following improvements over standard radiosurgical techniques:

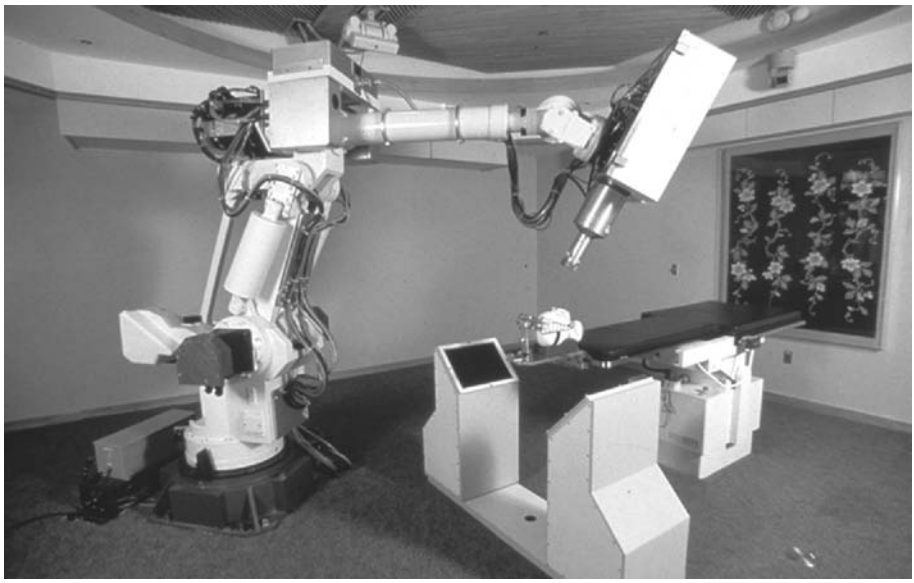

FIG. 15.3. Miniature linac mounted on an industrial robotic arm (CyberKnife). (Courtesy of Accuray, Inc.)

(i) It allows frameless radiosurgery (i.e. it dispenses with the need for a rigid and invasive stereotactic frame).
(ii) It monitors and tracks the patient's position continuously and uses on-line images for finding the exact position of the target in the treatment room coordinate system.
(iii) It aims the radiation beam into the on-line determined target position and achieves a dose delivery accuracy of the order of 1 mm through this image guided dose delivery method.
(iv) It allows for frameless radiosurgical dose delivery to extracranial targets such as the spine, lung and prostate through using the body skeleton or surgically implanted fiducial markers as a frame of reference for targeting.

15.2.6. Uncertainty in radiosurgical dose delivery

The minimum uncertainty in target localization achievable with modern imaging equipment combined with a frame based stereotactic technique is of the order of ±1 mm. The possible motion of brain tissues, when moving the patient from the imaging equipment to the therapeutic machine, is of the order of a fraction of a millimetre; thus of little concern.

The measured uncertainty in radiosurgical dose delivery for a linac in an excellent mechanical condition is of the order of ±0.5 mm, while for a gamma unit it is somewhat smaller, at ±0.3 mm. Both the gamma unit and the linac provide very similar overall accuracies in dose delivery; however, achieving and maintaining the optimal accuracy with an isocentric linac in comparison with a gamma unit requires a much larger effort as well as a very stringent and disciplined quality assurance programme. Owing to the intricacies of the specific dose delivery methods, the potential for serious problems, like a geographic miss, is greater on a linac than on a gamma unit. However, radiosurgery with isocentric linacs has a much greater potential for new developments than do gamma units; for example, computer controlled micro MLCs are already commercially available, allowing single isocentre treatments with irregularly shaped radiation fields.

A miniature linac mounted on a robotic arm not only offers a real potential for frameless radiosurgery and actual image guided dose delivery, with obvious benefits to the patient and staff, but also enables the use of stereotactic treatment techniques on organs other than the brain.

In comparison with multiple isocentre treatments, micro MLC treatments are simpler, use a single isocentre and result in dose distributions that are more homogeneous inside the target, conform better to the target shape and contribute a much lower scatter and leakage dose to radiation sensitive organs. Three dimensional conformal radiosurgery with modulated intensity fields produced with micro MLCs will become routinely used in clinics as soon as inverse treatment planning (ITP) software for radiosurgery becomes available.

15.2.7. Dose prescription and dose fractionation

The prescribed dose and fractionation of stereotactic dose delivery depend on the disease treated as well as on the volume and location of the intracranial target. Benign diseases are typically treated with a single session, while malignant tumours are treated with fractionated regimens.

Stereotactic radiosurgery (single session treatment):

- Is used in the treatment of functional disorders, vascular malformations, some benign tumours and metastatic lesions.
- Is occasionally used as a boost in conjunction with standard treatments of malignant intracranial lesions.
- Employs prescribed doses of 12–25 Gy; the larger the lesion, the lower the dose.

In stereotactic radiotherapy (fractionated treatment with stereotactic techniques) either the stereotactic frame is left attached to the patient's cranium for the duration of the treatment course or a relocatable stereotactic frame is used for individual treatments. The dose per fraction is typically larger than that of the standard treatment because of the complexities of radiosurgical treatments. Typical dose/fractionation regimens are: 6 × 7 Gy (total dose 42 Gy), with treatment given every second day, or 10 × 4 Gy (total dose 40 Gy), with treatment given daily.

15.2.8. Commissioning of radiosurgical equipment

The basic principles involved in the commissioning of radiosurgical devices are very similar for all such devices, despite the large variations in dose delivery techniques that they entail. The following issues should be considered before embarking on a clinical radiosurgical service:

- The properties of radiation beams must be measured to ensure radiation safety of the patient and accurate treatment planning;
- The mechanical integrity of the radiosurgical device must be within acceptable tolerances to provide reliable and accurate delivery of the prescribed dose;
- All steps involved in the radiosurgical procedure, from the target localization, through treatment planning to dose delivery, must be verified experimentally to ensure reliable and accurate performance of the hardware and software used in the radiosurgical procedure.

15.2.9. Quality assurance in radiosurgery

Stereotactic radiosurgery is a very complex treatment modality requiring not only close collaboration among the members of the radiosurgical team but also careful target localization and treatment planning, as well as strict adherence to stringent quality assurance protocols. The core radiosurgical team consists of a neurosurgeon, a radiation oncologist, a medical physicist and a radiotherapy technologist (radiation therapist).

The quality assurance protocols for radiosurgery fall into three categories:

- The basic quality assurance protocols covering the performance of all equipment used for target localization, 3-D treatment planning and radiosurgical dose delivery;

- The treatment quality assurance protocols dealing with the calibration and preparation of equipment immediately preceding the radiosurgical treatment;
- Treatment quality assurance during the radiosurgical procedure on a patient.

15.2.10. Gamma Knife versus linac based radiosurgery

The introduction of linac based radiosurgery in radiation oncology departments during the late 1980s has very rapidly transformed radiosurgery into a mainstream radiotherapeutic technique and has stimulated great advances in its technical and clinical utility. However, the move of radiosurgery into radiation oncology departments has also caused some problems and differences of opinion between neurosurgeons, who were the inventors and until then the principal users of radiosurgery, and radiation oncologists, who are the professionals trained and licensed in the treatment of disease with ionizing radiation.

Radiation oncologists are quite comfortable with the clinical use of isocentric linacs. They embraced the new linac based radiosurgical techniques with great enthusiasm, but had some reservations about the use of single high dose irradiation in radiosurgery, in contrast to the multifractionated schemes used in conventional radiotherapy. Neurosurgeons, however, had previous favourable experience with gamma unit radiosurgery and expressed serious concerns about the mechanical stability of isocentric linacs when used in radiosurgery.

An unstable linac isocentre could adversely affect the accuracy of dose delivery and result in substandard treatments in comparison with treatments provided by the 201 stationary beams from the gamma unit. These concerns are valid, and clearly not all isocentric linacs are suitable for conversion to radiosurgery. However, a well designed, well aligned and properly maintained isocentric linac will have a stable and small enough isocentre sphere (of the order of 1 mm diameter) to make it suitable for use in radiosurgery.

The general consensus among radiation oncologists and medical physicists is that linac based radiosurgical treatments with regard to treatment outcomes are equivalent to those provided by gamma units and that linac based techniques, in comparison with gamma units, are considerably more complicated but have a much greater potential for new and exciting developments.

The consensus among the majority of neurosurgeons is that the use of gamma units is superior to that of any linac based radiosurgical technique.

During the past decade this consensus has resulted in over 100 new gamma unit installations worldwide.

15.2.11. Frameless stereotaxy

In recent years great advances have been made in frameless stereotaxy, which aims to dispense with the invasiveness of the stereotactic frame fixation to the skull without losing the inherent accuracy of the frame based stereotactic approach. New techniques have been developed for image guided neurosurgery and radiosurgery based either on surgical implantation of fiducial markers (gold wire or screws) or on on-line planar imaging (linac on a robotic arm (see Section 15.2.5.3)).

The accuracy of target localization achieved with these new frameless techniques approaches that attainable with invasive stereotactic frames. Frameless radiosurgery relies heavily upon modern digital imaging and on-line monitoring, and is likely to replace the current frame based approach in the future.

15.3. TOTAL BODY IRRADIATION

TBI is a special radiotherapeutic technique that delivers to a patient's whole body a dose uniform to within ±10% of the prescribed dose. Megavoltage photon beams, either ^{60}Co γ rays or megavoltage X rays, are used for this purpose. In a broader sense, the treatment concepts of whole body irradiation encompass all irradiations with large photon fields, such as half-body irradiation, total nodal irradiation and irradiation of the whole body except for a few specific organs, which are partially or fully shielded from the prescribed dose.

15.3.1. Clinical total body irradiation categories

Depending on the specific clinical situation, TBI techniques are divided into the following four categories:

- High dose TBI, with dose delivery in a single session or in up to six fractions of 200 cGy each in three days (total dose 1200 cGy);
- Low dose TBI, with dose delivery in 10–15 fractions of 10–15 cGy each;
- Half-body irradiation, with a dose of 8 Gy delivered to the upper or lower half body in a single session;

- Total nodal irradiation, with a typical nodal dose of 40 Gy delivered in 20 fractions.

15.3.2. Diseases treated with total body irradiation

TBI is used primarily as part of a preparatory cytoreductive conditioning regimen prior to bone marrow transplantation (BMT). The source of marrow may be the patient (autologous transplant), an identical twin (syngeneic transplant) or a histocompatile donor (allogeneic transplant). In the near future, bioengineering promises to produce a supply of stem cells originating from unrelated and unmatched donors for use in bone marrow transplantation. The cells will be engineered so as to make rejection highly improbable, greatly expanding the usefulness and reliability of BMT.

Before engraftment of donor bone marrow, pretransplant conditioning is applied to eradicate the tumour cells or cells with genetic disorders. Although the conditioning regimen may be based on chemotherapy alone, the most common form of pretransplant conditioning is a combination of high dose chemotherapy and TBI. The latter is included in BMT protocols because it results in immunosuppression, which helps prevent the failure of the graft, a serious, usually fatal, complication of BMT, referred to as graft versus host disease. Thus an optimal application of TBI is a very important component of a successful BMT procedure.

The most notable diseases treated with BMT are:

- Various types of leukaemia (acute non-lymphoblastic, acute lymphoblastic and chronic myelogenous);
- Malignant lymphoma;
- Aplastic anaemia.

15.3.3. Technical aspects of total body irradiation

All contemporary TBI techniques use megavoltage photon beams produced by either ^{60}Co teletherapy units or linacs. The beams are either stationary, with field sizes of the order of 70×200 cm^2 encompassing the whole patient, or moving, with smaller field sizes, in some sort of translational or rotational motion to cover the whole patient with the radiation beam. Usually, parallel opposed irradiations are used by delivering each fractional dose in two equal instalments and switching the patient's position between the two instalments.

15.3.4. Total body irradiation techniques

TBI treatment techniques are carried out either with dedicated irradiators (Fig. 15.4(a) and (b) and Fig. 15.5) or, more commonly, with modified conventional megavoltage radiotherapy equipment. Currently, four methods are in use to administer TBI with modified conventional radiotherapy equipment:

- Treatment at extended source to surface distances (SSDs) (Fig. 15.4(c) and (d));
- Treatment at standard SSDs after the ^{60}Co machine collimator is removed (Fig. 15.5);
- Treatment with a translational beam (Fig. 15.6(a));
- Treatment with a sweeping beam (Fig. 15.6(b) and Fig. 15.7).

The first two techniques use large stationary beams and a stationary patient, while the latter two use moving beams produced by translating the

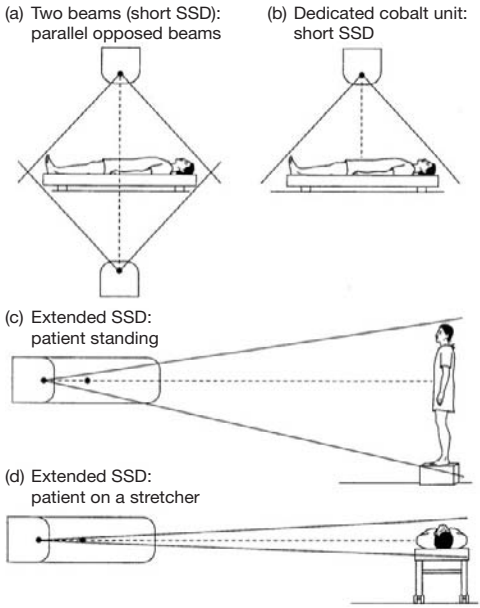

FIG. 15.4. Stationary beam TBI techniques: (a) two short SSD parallel opposed beams; (b) dedicated cobalt unit; (c) extended SSD — patient standing; (d) extended SSD — patient on a stretcher.

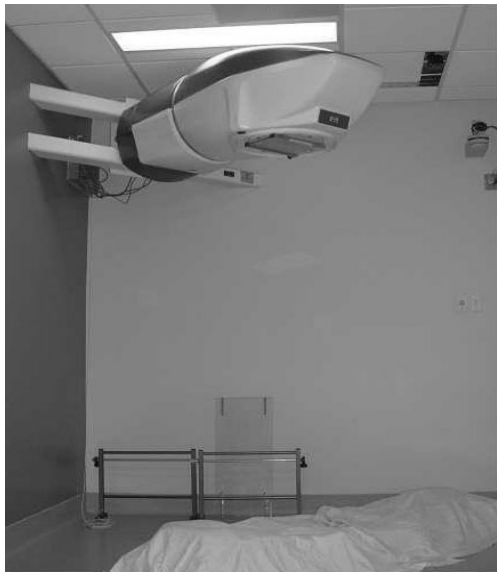

FIG. 15.5. A ^{60}Co teletherapy unit dedicated to TBI. The source to floor distance is 250 cm; the patient is treated on a floor mattress in a prone and supine position to obtain a parallel opposed beam.

patient through a stationary beam or through sweeping the beam over a stationary patient.

15.3.5. Dose prescription point

The TBI dose is prescribed to a point inside the body, referred to as the dose prescription point (usually at the midpoint at the level of the umbilicus). The TBI procedure must deliver the prescribed dose to the dose prescription point and should maintain the dose throughout the body within ±10% of the prescription point dose. Uniformity of dose is achieved with the use of bolus or compensators.

15.3.6. Commissioning of total body irradiation procedure

Once a particular treatment machine and TBI technique have been selected, a thorough commissioning of the proposed TBI procedure must be carried out. The basic dosimetric parameters for TBI are the same as those for standard radiotherapy, including absolute beam output calibration, percentage depth doses (PDDs) and beam profiles (off-axis ratios (OARs)). However,

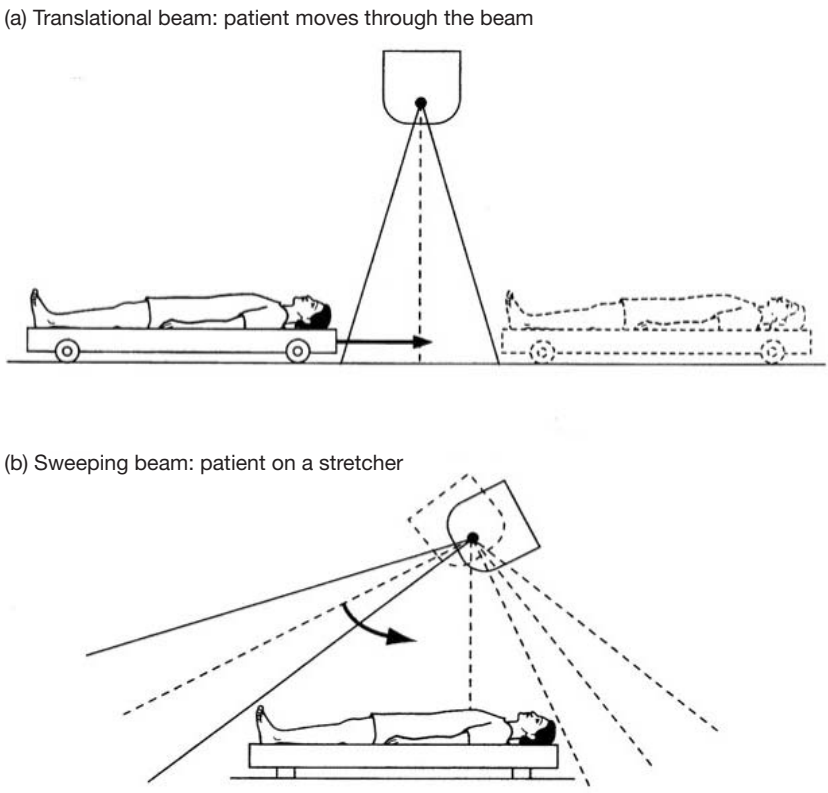

FIG. 15.6. Moving beam TBI techniques: (a) translational beam — patient moves translationally through a stationary beam; (b) sweeping beam — the beam sweeps over a stationary patient.

these parameters must be measured under the specific TBI conditions in order to obtain reliable data for use in clinical TBI.

Several dosimetric problems specific to large field dosimetry but not occurring in standard radiotherapy must be considered. These problems are related to the phantoms and ionization chambers that are used in the measurement of the dosimetric parameters. In contrast to standard radiotherapy, in TBI the phantoms are generally smaller than the actual field size and smaller than the patient. This causes different scattering conditions that might adversely affect the beam output as well as the PDDs required in the determination of the treatment times or monitor units (MUs) required to achieve the prescribed tumour dose.

The accuracy of the TBI dosimetric data might be adversely affected by the relatively large portion of the ionization chamber cable irradiated with the

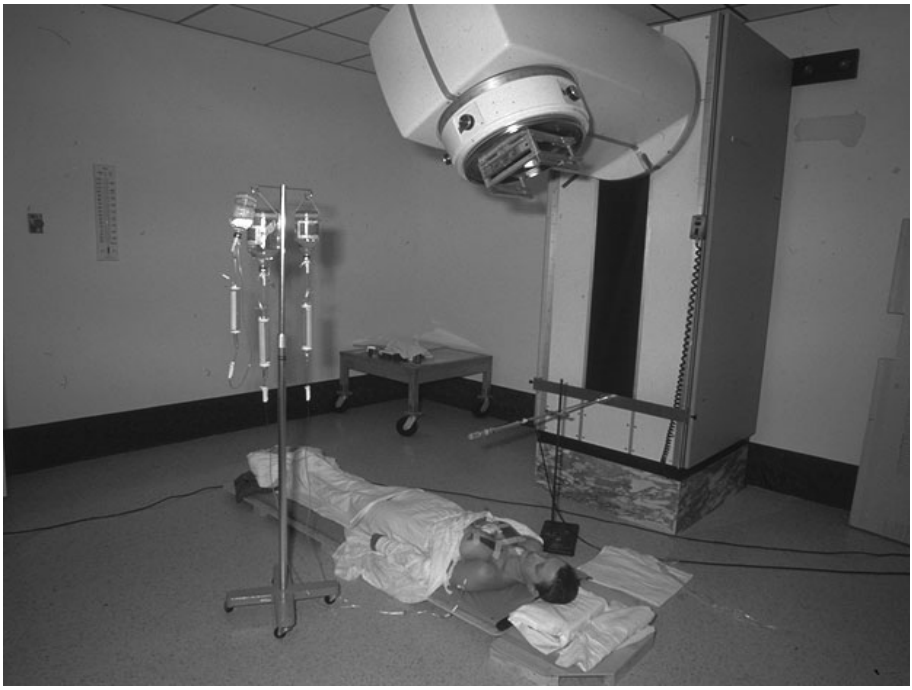

FIG. 15.7. Patient being treated with the sweeping beam TBI technique on a 4 MV linac.

large TBI field as well as by the chamber leakage currents and saturation characteristics, which become more problematic at the relatively low dose rates used in TBI.

15.3.7. Test of total body irradiation dosimetry protocol

Once the basic dosimetric data for a particular TBI technique to be used clinically are available, several TBI irradiation 'dry runs' should be carried out to verify the TBI dosimetry protocol.

15.3.8. Quality assurance in total body irradiation

TBI is a complex treatment modality requiring careful treatment planning, accurate localization of the organs that are to receive a reduced dose or to be shielded completely from the radiation beam and strict adherence to quality assurance protocols. These protocols fall into three categories: basic quality assurance, pretreatment quality assurance and treatment quality assurance.

- Basic quality assurance protocols cover the performance of the equipment used for TBI treatment planning and dose delivery. In addition to the dose delivery machine, which is either a cobalt unit or a linac, the TBI equipment may also include a CT scanner, which provides data on lung geometry and density as well as the geometry of other critical organs, and a TPS, which is used for the determination of lung dose.
- Pretreatment quality assurance protocols deal with calibration and with the preparation of equipment and the treatment room immediately preceding the TBI treatment. This includes positioning the equipment and any special TBI components such as flattening or compensating filters in the appropriate position as well as ensuring the proper functioning of any special dosimetric equipment that will be used for measuring the dose delivered to the prescription point or determining the transmission of radiation through the lung.
- Treatment quality assurance protocols deal with measurement of the dose delivered to the patient during the TBI procedure. The requirements for accurate dose delivery in TBI are as stringent as those in conventional external beam radiotherapy. It is important that in departments delivering TBI in vivo dose measurement techniques be available to verify the patient dose directly during the treatment or immediately after the first fractionated treatment.

15.4. TOTAL SKIN ELECTRON IRRADIATION

TSEI is a special radiotherapeutic technique that aims to irradiate the patient's whole skin with the prescribed radiation dose while sparing all other organs from any appreciable radiation dose. Since skin is a superficial organ, the choice of electron beams for the treatment of generalized skin malignancies (most commonly mycosis fungoides) is obvious, even though superficial X rays also could be, and actually were in the past, used for this purpose.

The patient population requiring TSEI is relatively small, therefore the technique is available only in major radiotherapy centres. In the past, superficial X ray machines, van de Graaff generators and even machines incorporating β particle emitting sources were used for TSEI. All contemporary TSEI procedures, however, are based on electron linacs, which are used for conventional radiotherapy and modified for delivery of the large and uniform electron fields required for TSEI.

Photon contamination of electron beams used in TSEI is a potential detriment to the patient. Its magnitude must therefore be known accurately for each particular TSEI technique to ensure that the total prescribed electron

beam dose to the patient's skin is not accompanied with an unacceptably high total body photon dose. Certain areas of the patient's skin as well as some organs (such as nails and eyes) may have to be shielded in order to avoid treatment morbidity. The typical dose/fractionation regimen is 40 Gy in 20 fractions.

15.4.1. Physical and clinical requirements for total skin electron irradiation

All clinical TSEI procedures are governed by three categories of specification:

- A physical specification of the large stationary electron field:
  - Electron field size of the order of 80×200 cm^2;
  - Dose uniformity at z_{max} in a water equivalent phantom for at least 80% of the central nominal field area (typically ±5% from dose at z_{max} in a phantom on the central ray);
  - Nominal SSD of 300–500 cm;
  - Beam energy at the waveguide exit window of 6–10 MeV;
  - Beam energy on the phantom surface of 4–7 MeV;
  - Dose rate on the beam central ray at z_{max} in a water equivalent phantom;
  - Photon contamination of the electron beam.
- A physical specification of the dose distribution resulting from the superposition of multiple stationary electron fields:
  - Dose rate at z_{max} on the central ray (usually on the skin surface, which becomes the dose prescription point);
  - Bremsstrahlung contamination dose rate at the patient's midpoint at the level of the umbilicus.
- Clinical specifications:
  - Dose/fractionation regimen;
  - Actual total body photon dose received by the patient during the course of the TSEI treatment;
  - Prescription for boosts to underdosed areas;
  - Prescription for any special shielding (eyes, nails, etc.).

15.4.2. Current total skin electron irradiation techniques

The TSEI techniques in use today may be grouped into three main categories:

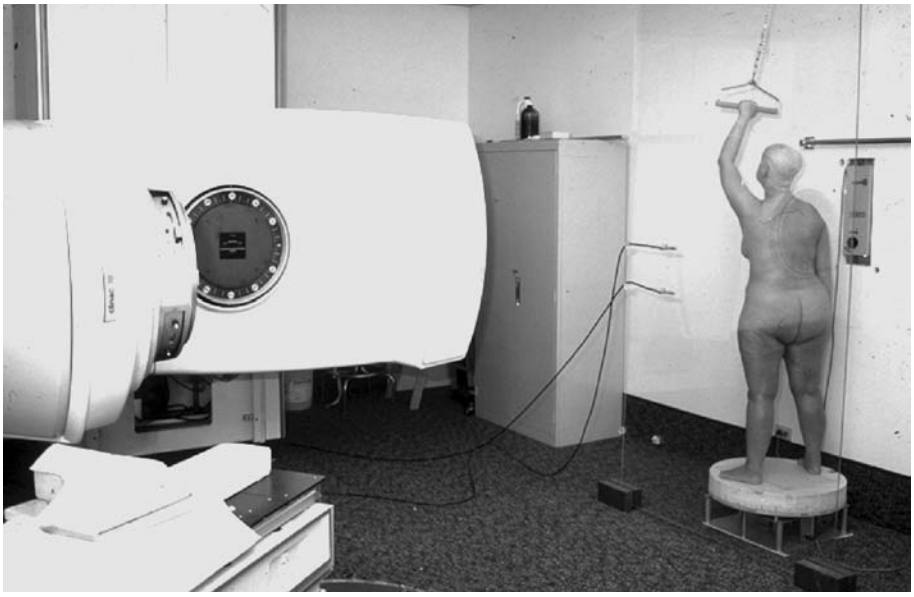

FIG. 15.8. Patient being treated for mycosis fungoides with the rotational TSEI technique.

- Translational techniques, in which the patient is translated on a stretcher through an electron beam of sufficient width to cover the patient's transverse dimensions;
- Large electron field techniques, in which a standing stationary patient is treated at a large SSD with a single large electron beam or a combination of large electron beams;
- Rotational techniques, in which the patient is standing on a rotating platform in a large electron field. A patient being treated with the rotational TSEI technique is shown in Fig. 15.8.

15.4.3. Selection of total skin electron irradiation technique

Once an institution decides to provide the TSEI treatment modality, an adequate TSEI technique must be chosen and commissioned, and quality assurance procedures for the clinical use of TSEI must be developed. The large electron field used for TSEI is produced either with single or dual electron fields; the patients will either be treated with multiple large electron beams or they will be rotated in a large electron beam.

15.4.4. Dose calibration point

The output of the large TSEI radiation field is specified at the dose calibration point, which is found on the electron beam central ray at z_{max} in a tissue equivalent phantom. Often the beam output and flatness are monitored directly on-line with two ionization chambers, one placed on the beam central axis to monitor the beam output and the other placed off-axis to monitor the flatness.

15.4.5. Skin dose rate at the dose prescription point

The TSEI dose is prescribed on the patient's skin surface at the level of the umbilicus (dose prescription point), which is usually on the axial slice containing the central ray. The dose rate at the dose prescription point is the skin dose rate resulting from the particular TSEI technique used in the treatment, be it with multiple stationary electron beams or with a rotational electron beam. The skin dose rate is related to the beam output at the dose calibration point, but the actual relationship for a particular technique must be determined experimentally.

15.4.6. Commissioning of the total skin electron irradiation procedure

Based on current TSEI standards, the TSEI technique, newly introduced into a clinic, will use a large and uniform stationary electron field and will treat the patient at a large SSD either with multiple beams in varying upright positions or by rotating an upright patient in a stationary electron beam. Various techniques involving the use of beam spoilers (to degrade the electron beam energy striking the patient) or special filters (to improve the electron beam flatness through electron beam scattering) are used to produce the large and uniform electron fields in the patient treatment plane.

For the purposes of TSEI procedure commissioning, a complete set of relevant dosimetric data must be collected, first for the large stationary electron field and then for the actual dose delivery with the multiple beams or the rotational beam.

The basic dosimetric parameters of the large TSEI electron field are:

- The field flatness measured at z_{max} in a tissue equivalent phantom and normalized to 100 at the dose calibration point;
- The electron beam output at the dose calibration point;
- PDDs measured to a depth of 15 cm in a tissue equivalent phantom.

The PDDs are normalized to 100 at the dose calibration point and measured on the beam central ray as well as on various directions parallel to the central ray. The physical characteristics of the clinical TSEI beam are measured with a modular cylindrical polystyrene or water phantom of 30 cm diameter and height. The skin dose rate is typically measured with thermoluminescence dosimetry or film on the phantom surface. The skin dose rate at the TSEI dose prescription point is given as a fraction of the calibration point dose rate, typically ranging from 0.4 to 0.5.

15.4.7. Measurement of clinical total skin electron irradiation dose distributions

In addition to the basic cylindrical dosimetry phantom, commissioning of the TSEI procedure should also involve measurements of dose distributions with an anthropomorphic body and head phantom augmented by various cylindrical tissue equivalent phantoms to simulate a complete patient, including legs and arms. This allows a thorough measurement of the skin dose distribution, of electron beam penetration into the body and of X ray contamination.

The shielding effects of legs upon each other and arms upon the head, neck and trunk should be evaluated, underdosed skin areas should be identified and boost irradiation methods should be developed to ensure that the whole patient's skin dose is as close as possible to the prescription skin dose.

15.4.8. Quality assurance in total skin electron irradiation

TSEI is a special technique that, much like any other irradiation procedure, requires strict adherence to quality assurance protocols. These protocols fall into three categories, similarly to the discussion in Section 15.3.8:

- A basic quality assurance protocol dealing with the equipment used in TSEI;
- A pretreatment quality assurance protocol dealing with the calibration and preparation of equipment immediately prior to the TSEI treatment;
- A treatment quality assurance protocol that deals with measurements of the actual dose delivered to the patient during the TSEI procedure.

15.5. INTRAOPERATIVE RADIOTHERAPY

IORT is a special radiotherapeutic technique that delivers in a single session a radiation dose of the order of 10–20 Gy to a surgically exposed internal organ, tumour or tumour bed. Thus IORT combines two conventional modalities of cancer treatment, surgery and radiotherapy, but, despite its long tradition, it is still a developing modality whose role in the management of many tumour sites remains to be determined.

Often IORT is applied as part of a treatment protocol that includes other modalities, such as chemotherapy and external beam radiotherapy. The initial treatments attempt to shrink the tumour, possibly simplifying the subsequent surgical resection. Typically, when surgical resection of a tumour mass is finally attempted, not all the tumour can be removed without significant morbidity. To improve local regional control, a large dose of radiation is delivered during the surgical procedure, with all or most radiosensitive normal tissues either shielded or displaced out of the radiation field.

15.5.1. Physical and clinical requirements for intraoperative radiotherapy

The IORT team consists of a surgeon, radiation oncologist, medical physicist, anaesthesiologist, nurse, pathologist and radiation therapist. IORT requires an operating room for the surgical procedure and a treatment room for delivery of the radiation dose. Often both rooms are merged into one, resulting in a specially shielded operating suite in which a dedicated radiation treatment unit is installed permanently.

Once a radiation modality and the location in which the treatment unit is to be installed are selected, an applicator system must be chosen. Applicators are important for three reasons:

- To define the target area;
- To shield tissues outside the target area from radiation;
- To keep sensitive tissues from falling into the target area during irradiation.

15.5.2. Intraoperative radiotherapy radiation modalities and techniques

There are three different radiation modalities that may be used to deliver radiation dose intraoperatively:

- Orthovoltage X rays;
- Megavoltage electron beams;
- High dose rate (HDR) ^{192}Ir brachytherapy sources.

The first treatment units used for delivering IORT were superficial and orthovoltage X ray units. While the initial treatment results were encouraging, the relatively poor penetration of X rays into tissue prevented a widespread development of X ray machine based IORT.

Most IORT programmes today are based on electron beams produced by megavoltage linacs, since electrons provide several advantages over X rays for the purposes of IORT:

— The electron dose is deposited over a definite range, thus sparing tissue downstream from the target;
— Depending on the target thickness and electron energy, the dose can be deposited homogeneously throughout the target volume;
— In contrast to low energy X rays, there is not much difference between the tissue and bone absorption of megavoltage electron beams.

15.5.3. Commissioning of an intraoperative radiotherapy programme

Once a decision is made on introducing an IORT service into an institution, an IORT team must be assembled, an IORT technique chosen and IORT equipment ordered.

Upon delivery of the equipment, the commissioning of the IORT procedure must be carried out:

- Radiation beam parameters must be measured and dosimetry data summarized so that they may be quickly understood and readily used. Dosimetry measurements that may be necessary, depending upon the IORT modality used, include: the absolute dose output at the end of treatment applicators; central axis depth dose data; the surface dose and buildup; bremsstrahlung contamination of electron beams if using the modality; and dose distribution data.
- The transition between the surgical procedure and irradiation must be carefully planned and all steps involved properly worked out and practised as part of the commissioning procedure. Irrespective of the radiation modality used for the IORT, the set of dosimetry data must be documented in an easily readable format to permit quick and accurate dosimetric calculations.

15.5.4. Quality assurance in intraoperative radiotherapy

Quality assurance for IORT treatments is in some respects even more important than that for standard radiotherapy, since IORT treatments are

almost always given in a single session, making it essentially impossible to correct a misadministration of dose.

Quality assurance in IORT consists of three components, similarly to the discussion in Section 15.3.8:

- Basic quality assurance dealing with all IORT equipment;
- Pretreatment quality assurance dealing with equipment preparation and verification immediately prior to the IORT treatment;
- Treatment quality assurance during the IORT dose delivery to the patient.

15.6. ENDOCAVITARY RECTAL IRRADIATION

In recent years increasing efforts have been directed towards the development of organ saving therapeutic approaches for malignant neoplasms, which were traditionally treated by radical surgery. For malignancies of the rectum and anal canal, sphincter saving procedures are successful in achieving not only a high probability of local control but also an improved quality of life by avoiding the permanent colostomy and male impotence that may result from abdominoperineal resection.

Endocavitary rectal (endorectal) irradiation is a sphincter saving procedure used in the treatment of selected rectal carcinomas with superficial X rays. The technique was introduced in the 1930s by Chaoul and subsequently developed and practised by others, most notably Papillon.

15.6.1. Physical and clinical requirements for endorectal irradiation

The main physical requirement for the technique to be successful is that the X ray beam should have a low effective energy, giving a PDD in tissue of 100% on the surface and about 50%, 30% and 10% at depths of 5, 10 and 25 mm, respectively. This implies an X ray tube potential of ~50 kVp and a short SSD treatment distance.

Selection criteria for endocavitary rectal irradiation are as follows:

- A biopsy proven, well or moderately well differentiated rectal adenocarcinoma;
- A mobile lesion with a maximum diameter of 3 cm;
- The location of the lesion within 10 cm from the anal canal;
- No evidence of lymph node or distant metastases.

Two techniques have been used for endorectal treatments:

— The short SSD technique, with the SSD of the order of 4 cm and the X ray tube inserted into the proctoscopic cone;
— The long SSD technique, with the SSD of the order of 20 cm and the X ray tube coupled to the cone externally.

Most of the published accounts of endorectal irradiation deal with the short SSD technique, which, in honour of its main proponent, is referred to as the Papillon technique. Both the proctoscopic cone and the inserted X ray tube are handheld during the treatment, making the treatment cumbersome, potentially unreliable because of possible cone movement during the treatment (geographical miss of the tumour) and, from the radiation protection point of view, potentially hazardous if proper radiation safety procedures are not followed.

The long SSD technique has been developed for use of superficial X ray tubes, the design of which does not allow insertion into a proctoscopic cone. However, there are in fact several advantages of long over short SSDs in endorectal irradiation:

(i) The X ray tube can be connected to the ~20 cm long proctoscopic cone externally, allowing the use of smaller diameter cones;
(ii) The X ray tube and the proctoscope do not have to be handheld during treatment, thereby improving positioning and treatment accuracy as well as solving the radiation protection problem;
(iii) The dose uniformity over the tumour volume is improved, since a change in SSD of a few millimetres on an irregular tumour surface affects the surface dose uniformity much more at an SSD of 4 cm than of 20 cm.

15.6.2. Endorectal treatment technique

The endorectal treatment technique consists of the following steps:

- The patient is positioned on the proctoscopic table and the proctoscopic cone with a plunger is inserted into the rectum;
- The plunger is removed, a proctoscopic viewing device is attached to the cone and the cone is placed over the tumour;
- In the short SSD technique the X ray tube is then inserted into the cone, and both the cone and the X ray tube are handheld for the duration of the treatment;

- In the long SSD technique the cone is then immobilized with an adjustable hydraulic clamp and the X ray tube is coupled with an electromagnetic lock to the cone and also immobilized;
- The X ray machine is turned on and the prescribed target dose is delivered.

The total tumour dose is of the order of 80 Gy and is delivered in two or three fractions of 20–30 Gy in each fraction. The fractions are typically given two weeks apart.

15.6.3. Quality assurance in endorectal treatments

Quality assurance in endorectal treatments is at least as important as in standard radiotherapy, since the number of fractions is relatively low and the prescribed dose per fraction is high.

The quality assurance in rectal irradiation consists of three components, similarly to the discussion in Section 15.3.8:

- Basic quality assurance dealing with the complete equipment consisting of the superficial X ray tube, treatment proctoscopic cone and obturator, and visualization device. The output of the X ray tube should be measured with a parallel-plate ionization chamber that is suitable for calibration of superficial X rays and has a calibration coefficient traceable to a standards laboratory. The effect of the chamber body on the chamber signal when the field size used in the calibration laboratory differs from the field size used clinically should be considered.
- Pretreatment quality assurance dealing with equipment preparation immediately prior to endocavitary treatment. Calibration of the X ray beam and operation of all other treatment components should be verified.
- Treatment quality assurance during the delivery of the endorectal treatment.

15.7. CONFORMAL RADIOTHERAPY

15.7.1. Basic aspects of conformal radiotherapy

The basic premise of conformal radiotherapy is that, in comparison with standard dose delivery techniques, tumour control can be improved by using special techniques that allow the delivery of a higher tumour dose while

maintaining an acceptable level of normal tissue complications. Conformal radiotherapy conforms or shapes the prescription dose volume to the PTV while at the same time keeping the dose to specified organs at risk below their tolerance dose. The conformal radiotherapy chain is based on 3-D target localization, 3-D treatment planning and 3-D dose delivery techniques.

Target localization is achieved through anatomical and functional imaging: CT, MRI, single photon emission computed tomography (SPECT), PET and ultrasound. Treatment planning is achieved either with standard forward planning techniques, which design uniform intensity beams shaped to the geometrical projection of the target, or, for more advanced conformal radiotherapy techniques, with inverse planning, which, in addition to beam shaping, uses intensity modulated beams to improve target dose homogeneity and spare organs at risk.

Dose delivery techniques range from the use of standard regular and uniform coplanar beams to intensity modulated non-coplanar beams produced with MLCs.

15.7.2. Multileaf collimators

Modern linacs can be equipped with MLCs that incorporate from 20 to 60 pairs of narrow, closely abutting tungsten leaves, each leaf projecting a typical width of 10 mm or less at the linac isocentre. MLCs projecting leaf widths of less than 5 mm at the isocentre are referred to as micro MLCs. They are used to shape irregular fields of less than 10 cm in maximal field dimension, such as head and neck fields, or irregular fields with less than 3 cm in maximal dimension, such as fields used in radiosurgery.

The MLCs may be an integral part of the linac head, replacing upper or lower secondary collimator jaws, or they may be attached to the linac head and used in conjunction with both the upper and lower collimator jaws. A typical MLC attached to a linac head and used in conjunction with the upper and lower collimator jaws is shown in Fig. 15.9.

Each leaf is individually motorized and computer controlled, allowing positioning with an accuracy better than 1 mm and the generation of irregular radiation fields, shaped to conform to the beam's eye view (BEV) target cross-section. A separate, miniature DC motor drives each leaf independently. Positional control and verification of the leaves is achieved by a sophisticated servomechanism using electronic or optical/video techniques to sense the position.

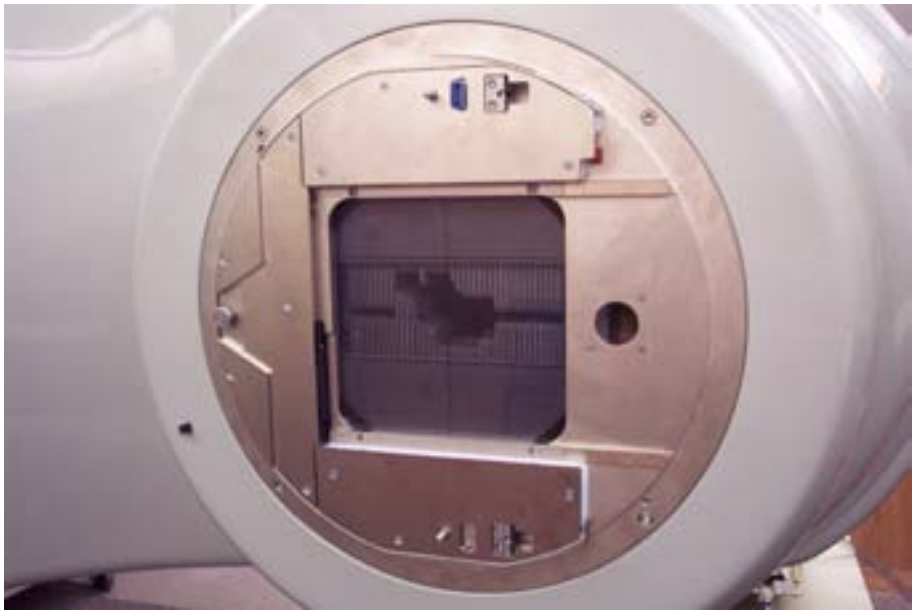

FIG. 15.9. MLC with 60 pairs of abutting tungsten leaves (Millenium MLC, Varian).

15.7.3. Acceptance testing of multileaf collimators

Before using an MLC clinically it is important that the user first carry out an elaborate acceptance testing protocol. Acceptance testing must cover the mechanical, radiation and software aspects of the MLC operation:

- Mechanical: the motion of the leaves and their maximum travel, abutting of the leaves on and off the central field axis, the alignment of MLC axes with axes of the linac secondary collimators, the positional reproducibility of the leaves, the interlocks for the leaves and jaw positional tolerances.
- Radiation: the transmission of the leaves, the leakage between the leaves, the leakage in the junction of two abutting leaves, both on the field axis and off the field axis, and the leaf penumbra both along the leaf and perpendicularly to it.
- Software: verification of the field shaper, the linkage between the TPS and the MLC and the accuracy of the field shaping and functioning of the controller.

15.7.4. Commissioning of multileaf collimators

The commissioning protocol involves obtaining a collection of beam data for all beam energies produced by the linac and various irregular fields produced by the MLC. The essence of the MLC commissioning is to verify that the physical characteristics of the MLC do not affect appreciably the basic dosimetric parameters of the open beams, such as field flatness, symmetry, collimator factor, output factor, scatter factor and PDD.

The in-phantom dosimetric parameters, such as the relative dose factor, scatter factor, PDD and tissue–maximum ratio (TMR), are determined by the field shape created by the MLC collimator. The in-air dosimetric parameter, the collimator factor, in linac configurations in which the MLC is essentially a tertiary collimator, is determined by the square or rectangular field shaped by the secondary linac collimator jaws and is considered independent of MLC shaping. In linac configurations in which the MLC replaces the upper or lower collimator jaws, the collimator factor is a function of the radiation field determined by the MLC.

15.7.5. Quality assurance programme for multileaf collimators

A quality assurance programme must be implemented for the clinical use of MLCs to ensure the reliable and safe operation of software and all mechanical components. The programme should cover positional accuracy, leaf motion reliability, leaf leakage, interlocks, networking and data transfer.

15.7.6. Intensity modulated radiotherapy

In addition to field shaping in 2-D conformal radiotherapy, in which the radiation fields are irregularly shaped but of uniform intensity, an MLC may also be used to achieve beam intensity modulation for use in 3-D conformal radiotherapy. From an obscure, highly specialized radiotherapeutic technique practised in only a few specialized centres around the world, IMRT has developed into a mainstream radiotherapeutic technique already available in most major radiotherapy centres around the world.

The IMRT technique is currently the most advanced form of conformal radiotherapy and holds great promise for improving radiotherapy both through increased tumour control probability and decreased treatment morbidity (i.e. decreased normal tissue complication probability (NTCP)). It relies on ITP for determination of the required intensity modulated beam maps and on 3-D multimodality imaging to define the target volumes.

In addition to CT, MRI and PET, ultrasound is beginning to play an important role because of its ease of incorporation into a treatment room, where the position of the target volume can be verified on a daily basis. However, the current routine clinical use of IMRT is still hindered by several difficulties, such as the:

- Complexity of the equipment used for dose delivery;
- Complexity of the ITP process;
- Quality assurance issues related to dose distribution calculation and dose delivery.

For IMRT planning the ITP techniques provide several advantages over the standard forward planning approaches, such as:

— Improved dose homogeneity inside the target volume and the potential for limited irradiation of surrounding sensitive structures;
— Increased speed and lesser complexity of the proposed solution;
— A quantitative introduction of cost functions, often incorporating dose volume constraints and biological functions;
— Adjustment of the optimal treatment planning to the actual dose delivery technique and accounting for all practical hardware limitations.

Various approaches to IMRT have been developed, ranging from simple standard physical compensators to scanned photon pencil beams. Between the two extremes are the currently used MLC based IMRT techniques, which fall into two categories: one uses multiple static MLC shaped fields and the other uses dynamic MLC dose delivery approaches.

Rudimentary IMRT treatments have been used clinically since the 1960s with wedges and physical compensators. Modern clinical IMRT, however, became possible in the latter part of the 1990s due to a synergistic effort among four areas that only then became well established:

(i) Three dimensional medical imaging by CT, MRI, SPECT and PET;
(ii) ITP;
(iii) Quality assurance techniques for verification of dose delivery;
(iv) Computer controlled dose delivery.

15.7.7. Commissioning of intensity modulated radiotherapy systems

The steps involved in the commissioning of an IMRT system will depend to some degree on the type of ITP system to be used. Some ITP systems are

simple modules within a standard 3-D TPS and use the regular dose calculation algorithm to evaluate the delivered dose from optimized fluence maps. To commission such a system it is necessary to first commission the standard TPS.

Extra measurements characterizing some basic properties of the MLC to be used must be made (e.g. leaf transmission and leakage, leaf maximum speed and other parameters specific to the ITP system). Other ITP algorithms are stand-alone systems that require complete beam data measurement, entry and possibly modelling, separate from a 3-D planning system. At least one manufacturer attempts to simplify the commissioning process by offering to carry out beam modelling for the customer, provided that all necessary beam data are supplied.

IMRT treatments can be delivered with the MLC operating in one of three basic modes:

- The segmented MLC (SMLC) mode, often referred to as the step and shoot mode;
- The dynamic MLC (DMLC) mode, sometimes referred to as the sliding window mode;
- Intensity modulated arc therapy (IMAT).

In the SMLC mode (static IMRT) the intensity modulated fields are delivered with a sequence of small segments or subfields, each subfield with a uniform intensity. The technique is also referred to as step and shoot, implying that the beam is only turned on when the MLC leaves are stationary in each of the prescribed subfield positions. There is no MLC motion while the beam is turned on.

In the DMLC mode (dynamic IMRT) the intensity modulated fields are delivered in a dynamic fashion with the leaves of the MLC moving during the irradiation of the patient. For a fixed gantry position the opening formed by each pair of opposing MLC leaves is swept across the target volume under computer control with the radiation beam turned on to produce the desired fluence map.

The new delivery method of IMAT has recently been proposed. In this method the sliding window approach is used as the gantry rotates around a patient. IMAT should result in the most conformal dose distributions possible with standard linac hardware.

Each method of delivery needs to be commissioned separately, as the MLC and linac performance is stressed differently depending on the method. IMRT treatments require tighter tolerances on MLC performance than required when the MLC is to be used only in static applications. Thus a set of commissioning tests separate from those described earlier for the MLC alone

needs to be developed. These tests must be able to verify the accuracy and reproducibility of MLC positioning and movement for each delivery technique to be used clinically.

Often a clinic will adopt a single delivery method to allow all staff members to become proficient in its principles and to avoid confusion. This simplifies the commissioning process, since only one delivery method needs to be tested.

Verification of the accuracy of the dose calculation algorithm of an inverse planning system is carried out using the standard dosimetry tools (radiographic or radiochromic film, thermoluminescence dosimetry, ionization chamber in conjunction with various phantoms). Most commercially available IMRT planning systems permit fluence maps optimized for a clinical application to be transferred to a representative phantom for calculation. The phantom can be then physically loaded with any of the above mentioned dosimeters and irradiated with the planned IMRT fields.

Many phantoms specially designed for verification of IMRT fields have recently become commercially available. These phantoms have various inhomogeneities built in that allow verification not only of IMRT plans but also of the algorithm used for tissue inhomogeneity corrections. It is also possible, however, to use simple phantoms made of Lucite, polystyrene or other water equivalent materials, in which dosimeters can be positioned but no inhomogeneities (heterogeneities) can be accounted for.

15.7.8. Quality assurance for intensity modulated radiotherapy systems

A comprehensive quality assurance programme must be developed to ensure accurate IMRT dose delivery. This programme must include standard verification of accelerator radiation output as well as testing of dynamic MLC positioning and movement. A good approach is to perform a subset of the commissioning tests on a regular basis. Owing to the added stress on MLC components, particularly the motors, it is recommended to augment the standard spare parts kit to include at least several additional motors.

15.7.9. Dose verification for intensity modulated radiotherapy treatment plans

It is strongly recommended to carry out an independent verification of all IMRT treatment plans, at least until the entire IMRT team is comfortable with the planning and treatment delivery processes. This is done through a transfer of each IMRT plan to a representative phantom for dose calculation. The phantom can then be loaded with various dosimeters and irradiated with the

IMRT fields planned for the patient. Actual dose delivery can then be compared with the plan and evaluated for accuracy. Several manufacturers have recently developed software and hardware that greatly simplify the evaluation of IMRT dose delivery. These systems should be seriously considered for purchase in addition to any IMRT software/hardware system.

15.8. IMAGE GUIDED RADIOTHERAPY

Over the past decade there have been substantial advances in the technology used to plan and deliver precision radiotherapy. ITP and virtual simulation, which are aided by fusion of multimodality images (CT, MRI and PET) of patient anatomies, have revolutionized the planning of radiotherapy treatments. In the near future determination of intratumoural volumes that need to be treated with extra high doses, such as hypoxic cells or cells with low intrinsic radiosensitivity, will become possible through the rapidly developing molecular imaging technology.

In parallel with developments in target localization, the efficacy of treatment delivery has been improved with the recent introduction of IMRT and tomotherapy. The accuracy of dose delivery with these new techniques has been limited by uncertainty in target localization at the time of treatment. Interfraction as well as intrafraction target movement relative to reference landmarks coupled with set-up errors and other inaccuracies add to this uncertainty. The standard approach has been to add margins to the target volume, usually at the expense of most of the potential benefits of the more precise treatment delivery techniques.

It has recently become possible to image patient anatomy just before delivery of a fraction of radiotherapy, thus gaining precise knowledge of the location of the target volume on a daily basis. This technique of dose delivery to the patient is known as IGRT and has the potential of ensuring that the relative positions of the target volume and some reference point for each fraction are the same as in the treatment plan. This may allow reduced treatment margins, fewer complications, dose escalation and the avoidance of geographical misses.

The ideal image guided system will allow the acquisition of soft tissue images at the time of each fraction of radiotherapy. The system must be fast and simple so as not to affect appreciably the patient throughput on the treatment machine, be accurate within the limits of target definition and have the ability to deliver a conformal dose.

Several IGRT systems are currently commercially available. All systems allow pretreatment imaging immediately after a patient is positioned on the

linac treatment table for therapy. These IGRT systems are based on direct integration of:

- A kilovoltage or megavoltage imaging system with an isocentric medical linac, referred to as cone beam computed tomography (CBCT) and offered by two linac manufacturers as onboard imaging options: Elekta (Synergy model) and Varian (Trilogy model).
- A CT scanner integrated with an isocentric medical linac, offered by Siemens (Primatom model).
- Megavoltage computed tomography (MVCT) with a tomotherapy machine that uses a miniature linac waveguide mounted on a CT type gantry, offered by TomoTherapy, Inc.
- A 2-D or 3-D ultrasound imaging system integrated with an isocentric medical linac, manufactured by Nomos (BAT system) and BrainLab (ExacTrac system).
- On-line imaging with paired orthogonal planar imagers with a miniature linac mounted on a robotic arm, offered by Accuray (CyberKnife system).

15.8.1. Cone beam computed tomography

CBCT imaging enables visualization of the exact tumour location just prior to patient treatment on a linac. The technique integrates CT imaging with a linac and involves acquiring multiple planar images produced by a kilovoltage or megavoltage cone beam rotating a full 360º about the patient in the treatment position on the linac table. A filtered backprojection algorithm similar to CT scanning algorithms is used to reconstruct the volumetric images of the target volume, sensitive structures and landmarks in the patient. The volumetric data are then compared with the planning CT data as well as the associated optimized dose distribution, and a decision is made on fine tuning the patient position to account for tumour motion or set-up error.

Both kilovoltage and megavoltage beams can be used for CBCT:

- The kilovoltage system consists of a conventional X ray tube mounted on a retractable arm at 90º to the high energy treatment beam and a flat panel X ray detector mounted on a retractable arm opposite the X ray tube. The X ray system can, in addition to cone beam images, produce radiographic and fluoroscopic images.
- The advantage of megavoltage beams for CBCT is that the beams come from the linac beam line and thus no additional equipment is required to produce the cone beam; however, kilovoltage beams produce better soft

tissue contrast and are thus deemed more useful. A megavoltage CBCT makes use of the detector panel that is already present for use in electronic portal imaging.

Elekta and Varian linacs equipped with onboard imaging for CBCT are shown in Figs 15.10 and 15.11.

15.8.2. Computed tomography Primatom

A system comprised of a linac and a CT unit at opposite ends of a standard radiotherapy treatment table has been developed and is marketed by Siemens. This system allows precise CT imaging of patient anatomy prior to each fraction of radiotherapy. Not only can the patient be shifted to compensate for target motion and set-up inaccuracies, but the system can also in principle allow clinicians to account for changes in target volume size and shape over a multifraction course of radiotherapy.

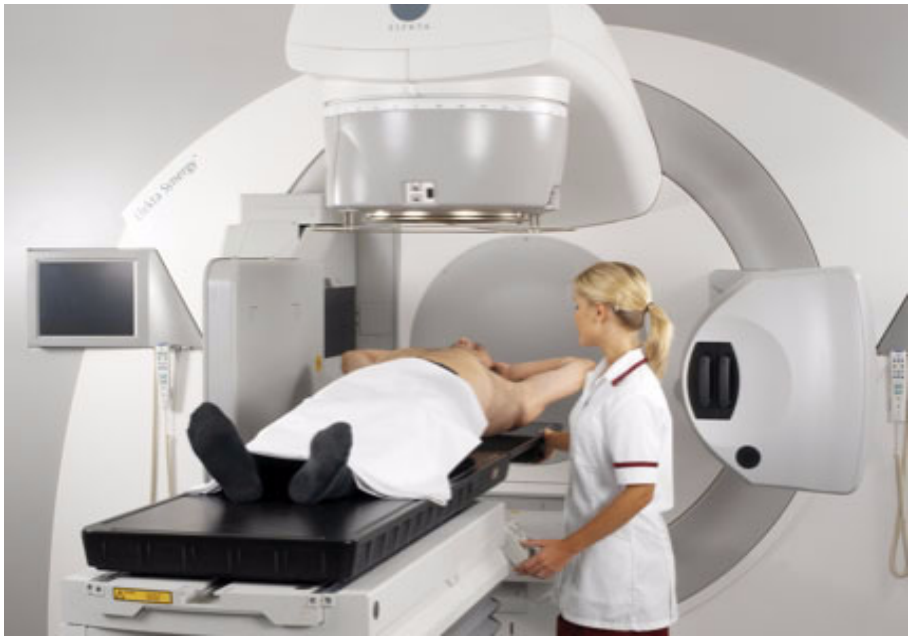

FIG. 15.10. The onboard X ray imaging system for CBCT integrated into an Elekta Synergy linac system. (Courtesy of Elekta AB.)

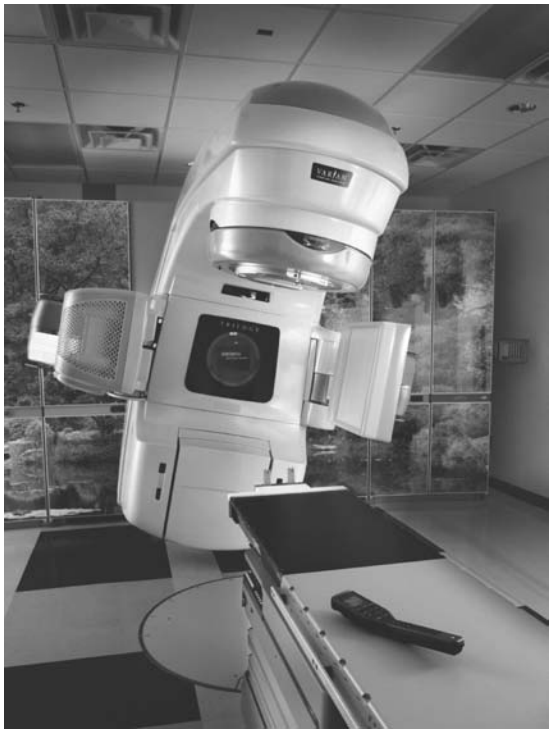

FIG. 15.11. The onboard X ray imaging system for CBCT integrated into a Varian Trilogy linac system. (Courtesy of Department of Radiation Oncology, Emory University School of Medicine, Atlanta, Georgia, USA. Photo by Weinberg-Clark Photography.)

15.8.3. Tomotherapy

The tomotherapy concept for delivering radiotherapy was introduced in the early 1990s at the University of Wisconsin. Since then many research publications have demonstrated the potential benefit of delivering radiation dose using this innovative approach. A commercial version, known as the TomoTherapy HI ART System, was released recently for clinical use and combines treatment planning, patient positioning and dose delivery into one system.

In the tomotherapy system, IMRT is delivered with a 6 MV linac that is mounted on a CT type gantry ring, allowing the linac to rotate around a patient. Beam collimation is accomplished with a computer controlled MLC, also on the rotating gantry, that has two sets of interlaced leaves that rapidly move in and out of the beam to constantly modulate the intensity of the radiation beam

as the linac rotates around the patient. During treatment, the table advances the patient through the gantry bore so that the radiation dose is delivered in a helical geometry around the target volume.

The system is designed to obtain an MVCT scan of patient anatomy at any time before, during or after treatment. The MVCT image data are acquired with a 738 element xenon ionization chamber array that rotates on the gantry opposite the linac. This image guidance allows fine adjustment of the patient's position at every fraction to ensure that the dose distribution will be delivered precisely to the target volume as planned. A CT scan can also be taken immediately after a fraction of therapy with the patient still in the treatment position, allowing, at least in principle, an evaluation of the true dose distribution delivered to the patient.

15.8.4. BAT system

Nomos introduced the BAT (B-Mode Acquisition and Targeting) system. The system consists of a cart based ultrasound unit positioned next to a linac treatment table and is used by a radiotherapist to image the target volume prior to each fraction of a patient's radiotherapy. The relationship of the target volume to a reference point, usually the linac isocentre, is determined interactively by the user and compared with the target volume originally contoured in the CT data set. Suggestions for patient translation to move the target volume into the same position relative to the isocentre as in the treatment plan are made by the system, and the therapist can then move the patient, based on this information, to gain better treatment accuracy.

The BAT system has found its widest application in pelvic radiotherapy, particularly for prostate cancer. The prostate can move significantly from one day to another within the pelvis relative to bony anatomy. Imaging the prostate target volume transabdominally with an ultrasonic probe on a daily basis and fine tuning the patient position based on system suggestion permits an accurate delivery of conformal treatment plans and allows target dose escalation without causing unacceptable bladder and rectal complications.

15.8.5. ExacTrac ultrasonic module

BrainLab has also developed an ultrasound based system for IGRT to be used in conjunction with an isocentric linac. This system can be used with any ultrasound unit, and is comprised of a reflective marker array attached to an ultrasound probe. This array is calibrated by the ExacTrac infrared tracking system relative to reflective markers attached to the patient's body. In principle, the system works similarly to the BAT system described above, and

allows fine adjustment of the patient's position to compensate for target movement and set-up inaccuracies.

15.8.6. CyberKnife

The CyberKnife was developed in the mid 1990s by Accuray as an innovative tool for intracranial stereotactic radiosurgery (see Section 15.2.5.3). It delivers the dose with a miniature (10^4 MHz) linac mounted on an industrial robotic arm, a combination that offers excellent spatial accuracy in dose delivery and allows, in comparison with isocentric linacs and tomotherapy units, a great deal of flexibility in directing the beam towards the target.

Owing to its on-line target imaging and automatic adjustment of the radiation beam direction to compensate for target motion, the CyberKnife provides a frameless alternative to conventional radiosurgical procedures. The rigid invasive stereotactic frame, the essential component of standard radiosurgical treatments used for target localization, treatment set-up and patient immobilization during treatment, is not required for treatment with the CyberKnife.

The location of the lesion is predetermined through a family of axial CT images that serves as a base for the determination of a set of digitally reconstructed radiograph (DRR) images. A set of paired orthogonal X ray imagers determines the location of the lesion in the room coordinate system and communicates these coordinates to the robotic arm, which adjusts the pointing of the linac beam to maintain alignment with the target.

The CyberKnife radiosurgery system provides an innovative approach to image guided dose delivery that is based on an on-line orthogonal pair of digital X ray imagers, a patient CT data set fused with MR and/or PET images and a miniature linac mounted on an industrial robotic arm. This new approach to highly accurate intracranial as well as extracranial delivery of high radiation doses with small radiation fields opens the field of radiosurgery to very exciting new research directions, both in basic radiation physics and clinical cancer research.

Besides the obvious advantage of dispensing with the need for a stereotactic frame without compromising the treatment's spatial accuracy, the CyberKnife also offers several other advantages over conventional radiosurgery, such as:

- Veritable image guided dose delivery.
- Possibility for fractionated treatment of intracranial malignant tumours.
- Possibility for treatment of extracranial spinal lesions, relying on the skeleton to provide a reference frame.

- Possibility for radiosurgical treatment of other organs such as the lung and prostate using surgically implanted fiducial markers as a reference frame.
- Capability for on-line tracking of target motion, which results either from patient motion during treatment or from organ motion within the patient during treatment.

15.9. ADAPTIVE RADIOTHERAPY

A full implementation of IGRT will lead to the concept of adaptive radiotherapy (ART). In this process the dose delivery for subsequent treatment fractions of a course of radiotherapy can be modified to compensate for inaccuracies in dose delivery that cannot be corrected for by simply adjusting the patient's positioning. The causes of these inaccuracies may include tumour shrinkage, patient loss of weight and increased hypoxia resulting during the course of fractionated treatment.

15.10. RESPIRATORY GATED RADIOTHERAPY

In the current radiotherapy practice relatively large margins are added to tumour volumes in the chest and upper abdominal cavities to compensate for the effects of respiratory motion on tumour dose delivery. This results in compromises to prescribed tumour doses as well as treatment plans that adversely affect the treatment outcome and increase the incidence of radiation induced morbidity. The quest for ever increasing tumour doses to increase the tumour control probability (TCP) combined with the goal of low NTCP results in smaller margins around the tumour and a need to deal effectively with organ motion during the treatment.

The next big challenge in IGRT thus comes from the natural and unavoidable organ motion during treatment. To account for this organ motion 4-D imaging technology is required, which allows viewing of volumetric CT images changing over the fourth dimension, time. For example, image guided radiosurgery, discussed above, is an elegant, albeit not the only, approach to dealing with organ motion. A simpler means is provided by the respiratory gating system (RGS), which is a special accessory added to a linac to compensate automatically and instantly for the effects of respiratory movement on external beam radiotherapy to the chest and upper abdomen.

Respiratory gated treatment was developed in Japan for radiotherapy with heavy ions, and the idea was recently introduced to treatment with linacs.

Varian developed an RGS that is referred to as a real time position management RGS and is applicable to any organ or structure subject to respiration induced motion, such as the breast, lung, mediastinum, liver and pancreas. The system is non-invasive, allows dose escalation combined with tighter tumour margins and can also be used in IMRT and other 3-D conformal treatments. A reflective marker is placed on the patient's chest and a video camera tracks its up and down movement. The continuous marker signal is processed by a computer that initiates a beam hold in the linac when the breath movement exceeds parameters that were determined during the treatment simulation. The target motion is correlated with the motion of external markers in simulation and these markers are then used in the treatment to control appropriate beam-on times to limit treatment to those time periods when the target is static.

Elekta developed the Active Breathing Coordinator (ABC), which allows clinicians to deliver radiation dose to the patient during the breath hold. The breathing volume is measured by the machine's mouthpiece and the pattern is displayed on the control room monitor. When the breath hold volume is achieved, a balloon valve is actuated to block airflow to the patient for a predetermined period of time. The end result is a repeatable breath hold that provides the same volumes each time. The operator irradiates during this breath hold, reducing the motion of the tumour during irradiation.

15.11. POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY SCANNERS AND POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IMAGE FUSION

PET/CT machines combining the strengths of two well established imaging modalities represent the most exciting innovation in cancer diagnosis and therapy of the late 1990s. Both PET and CT have been used as imaging modalities since the early 1970s. This section discusses some characteristics of each individual unit, demonstrating the rationale behind the development of the combined PET/CT scanner.

The CT scanner was invented by Hounsfield and Cormack and is based on acquisition of a large number of cone beam projections around a patient by a detector array and representation of transmission measurements of X rays through a patient. The measured transmission data are reconstructed to produce a tomographic image, most commonly through the filtered backprojection method.

The usefulness of CT in radiotherapy was recognized almost immediately after its development, and it has been used not only for providing a detailed

image of internal anatomy, including tumour volumes, but also for providing electron densities for the accurate treatment planning of tissues with heterogeneities.

CT yields a detailed image of the body's anatomical structures by producing cross-sectional X ray slices of the body. While CT is excellent in depicting structures and anatomy, it may miss small or early stage tumours, and, moreover, it does not provide any functional information on the tumours it detects.

PET provides information on the metabolic function of organs or tissues by detecting how cells process certain compounds such as glucose. Most cancer cells metabolize glucose at a much higher rate than normal tissues. By detecting increased radiolabelled glucose metabolism with a high degree of sensitivity, PET identifies cancerous cells, even at an early stage, when other imaging modalities may miss them.

Owing to its relatively poor spatial resolution, PET cannot pinpoint the exact size and location of tumours to the precision required for optimal diagnosis and treatment planning. This limitation until recently precluded a wider use of PET machines in radiotherapy.

In a typical PET study, one administers a positron emitting radionuclide by injection or inhalation. The radionuclide circulates through the bloodstream to reach a particular organ. The positrons emitted by the radionuclide have a very short range in tissue and undergo annihilation with an available electron. This process generally results in an emission of two γ rays, each with an energy of 0.511 MeV, moving away from the point of production in nearly opposite directions (at 180º to each other).

The PET machine generates transverse images depicting the distribution of positron emitting radionuclides in the patient and uses annihilation coincidence detection to obtain projections of the activity distribution. The transverse images are obtained through the process of filtered backprojection.

Detectors used for coincidence detection in modern PET machines are scintillators made of bismuth germanate (BGO) or lutetium oxyorthosilicate doped with cerium (LSO:Ce) that transform the 0.511 MeV γ ray energy into visible photons detected by photomultiplyer tubes (PMTs).

The radionuclides used in PET studies are produced by bombardment of an appropriate stable nuclide with protons from a cyclotron (see Section 5.4), thereby producing positron emitting radionuclides that are subsequently attached to clinically useful biological markers. The common positron emitting radionuclides used in PET imaging studies are listed in Table 15.1.

The ^{18}F radionuclide attached to the 2-fluoro-2-deoxy-D-glucose (FDG) molecule is the biological marker most commonly used in studies involving glucose metabolism in cancer diagnosis and treatment.

TABLE 15.1. COMMON POSITRON EMITTING RADIONUCLIDES USED IN POSITRON EMISSION TOMOGRAPHY

Radionuclide	Symbol	Half-life (min)	Maximum positron energy (keV)
Carbon-11	C-11	20.5	960
Nitrogen-13	N-13	10	1200
Oxygen-15	O-15	2	1732
Fluorine-18	F-18	110	634
Rubidium-82	Rb-82	1.2	3356

The relatively short half-life of the positron emitting radionuclides used in PET scanning requires that a cyclotron be available near the PET machine, making a routine PET scanning clinical service very costly.

PET and CT obviously complement each other in providing important diagnostic information. Separate PET and CT images are unfortunately difficult to fuse because the patient is generally not positioned identically on both machines. However, the recently introduced PET/CT machines, integrating PET and CT technologies into a single device, enable the collection of both anatomical and biological information simultaneously during a single examination, resulting in accurately fused PET and CT images that permit a more accurate tumour detection and tumour localization for a wide variety of cancers.

The main advantages of PET/CT machines are as follows:

- Earlier diagnosis of disease;
- Accurate staging and tumour localization;
- More precise treatment;
- Monitoring of response to treatment and early detection of recurrences;
- Reduction of biopsy sampling errors;
- Reduction of the number of invasive procedures required during follow-up.

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