CHAPTER 15.

SPECIAL PROCEDURES AND TECHNIQUES IN RADIOTHERAPY

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15.1. INTRODUCTION

In addition to routine conventional radiotherapy techniques used in standard radiotherapy departments and clinics, several specialized techniques are known and used for special procedures. These techniques deal with specific problems that usually require equipment modifications, special quality assurance procedures, and heavy involvement and support from clinical physicists. Because of their increased complexity and the relatively low number of patients who require them, these specialized techniques are usually available only in larger, regional centers.

The radiotherapy techniques that currently fall into the specialized category are:

1. Stereotactic irradiation
2. Total Body Irradiation (TBI) with photon beams
3. Total Skin Electron Irradiation (TSEI)
4. Intraoperative radiotherapy (IORT)
5. Endorectal irradiation
6. Conformal radiotherapy and Intensity Modulated Radiotherapy (IMRT)
7. Image-Guided Radiation Therapy
8. Respiratory Gated Radiation Therapy
9. PET/CT fused images

15.2. STEREOTACTIC IRRADIATION

From an obscure irradiation technique practiced in the 1960s and 1970s in only a few specialized centers, stereotactic irradiation has during the past 15 years developed into a mainstream radiotherapeutic technique practiced in most major radiotherapy centers around the world. Stereotactic irradiation is the term used to describe focal irradiation techniques that 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.
Main characteristics of stereotactic irradiation are as follows:

- Total prescribed doses are on the order of 10 Gy to 50 Gy and the planning targets are small with typical volumes ranging from 1 cm$^3$ 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, external beam stereotactic irradiation 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 was found useful for external beam radiotherapy has also found use in radiosurgery (cobalt gamma rays, megavoltage x rays, proton and heavy charged particle beams, and even neutron beams).

### 15.2.1. Physical and clinical requirements for radiosurgery

- Accurate determination of 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 which 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 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 in 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

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

15.2.3. Equipment used for stereotactic radiosurgery

- **Stereotactic frame** which defines a fixed coordinate system for an accurate localization and irradiation of the planning target volume. The stereotactic frame is also used for patient setup on the treatment machine and for patient immobilization during the actual treatment procedure.

- **Imaging equipment** (CT, MR, DSA) with which the structures, lesions and planning target volumes 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.

- **Treatment planning system** with which the 3D dose distribution for the radiosurgical treatment is calculated and superimposed on the patient's anatomical information.

- Appropriate radiation source and radiosurgical treatment technique.

15.2.4. Historical development

- The combined use of stereotaxy and irradiation in 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 focussed cobalt-60 gamma rays, and more recently to megavoltage x rays from linear accelerators.

- Linacs were proposed as viable radiation sources for radiosurgery in 1974 by Larsson. In 1984 Betti and Derechinsky from Buenos Aires reported on the development and clinical application of the linac-based *multiple noncoplanar 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 nonconverging arcs technique, while McGill developed its own radiosurgical technique, referred to as the dynamic stereotactic radiosurgery.

15.2.5. Radiosurgical techniques

The **Gamma knife** (Elekta, Stockholm, Sweden) is a radiosurgical device that has been associated with, and dedicated to, radiosurgery for the past 35 years. Despite great technological advances during this time, the fundamental design and principles of the Gamma unit have not changed much since the Swedish neurosurgeon Leksell introduced the prototype unit in the late 1960s. The unit incorporates 201 cobalt-60 sources housed in the central body of the unit. These sources produce 201 collimated beams directed to a single focal point at a source-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:

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

*FIG. 15.1. A Gamma Knife installation showing the main body of the unit containing 201 cobalt sources (at 30 Ci = 1.11×10¹² Bq each source), the treatment couch and a collimator helmet attached to the treatment couch.*
**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 the small diameter circular radiosurgical beams or a micro-multileaf collimator (micro-MLC) to define the small area irregular fields;
- remotely controlled motorized couch or treatment chair rotation;
- couch brackets or a floor stand for immobilizing the stereotactic frame during treatment;
- inter-locked readouts for angular and height position of the couch; and
- special brakes to immobilize the vertical, longitudinal, and lateral couch 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 (couch or chair) from given start to stop angles. In the multiple non-coplanar converging arcs technique the patient is stationary either on the treatment couch 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 300° from 30° to 330° and couch 150° from 75° to −75°). 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.

*FIG. 15.2. Patient treated with the dynamic stereotactic radiosurgery technique.*
• **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.

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

1. It allows frameless radiosurgery, *i.e.*, it dispenses with the need for a rigid and invasive stereotactic frame.

2. It monitors and tracks the patient position continuously and uses on-line images for finding the exact position of the target in the treatment room coordinate system.

3. It aims the radiation beam into the on-line determined target position and achieves a dose delivery accuracy on the order of 1 mm through this image-guided dose delivery method.

4. It allows for frameless radiosurgical dose delivery to extracranial targets, such as spine, lung and prostate, through using the body skeleton or surgically implanted fiducial markers as a frame of reference for targeting.

*FIG. 15.3. Miniature linear accelerator mounted on an industrial robotic arm.*
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 on the order of ±1 mm. The possible motion of brain tissues, when moving the patient from the imaging equipment to the therapeutic machine, is on the order of a fraction of a millimeter; thus of little concern.

The measured uncertainty in radiosurgical dose delivery for a linac in an excellent mechanical condition is on the order of ±0.5 mm, while for a Gamma unit it is somewhat smaller at ±0.3 mm. Both the Gamma unit and linac provide very similar overall accuracies in dose delivery; however, achieving and maintaining the optimal accuracy with an isocentric linac in comparison to a Gamma unit requires a much larger effort as well as a very stringent and disciplined quality assurance program. Because of 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.

On the other hand, radiosurgery with isocentric linacs has a much greater potential for new developments than does the Gamma unit. For example, computer-controlled micro-multileaf collimators are already commercially available, allowing single isocenter treatments with irregularly-shaped radiation fields.

The 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-isocenter treatments, the micro-MLC treatments are simpler, use a single isocenter, and result in dose distributions which 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. The 3D conformal radiosurgery with modulated intensity fields produced with the micro-MLC will become routinely used in clinics as soon as inverse treatment planning 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)
  - used in treatment of: functional disorders, vascular malformations, some benign tumours, and metastatic lesions.
  - occasionally used as a boost in conjunction with standard treatment of malignant intracranial lesions.
  - prescribed doses: 12 Gy to 25 Gy; the larger is the lesion, the lower is the dose.
• **stereotactic radiotherapy** (fractionated treatment with stereotactic techniques)

  - the stereotactic frame is left attached to patient's cranium for the duration of the treatment course or a relocatable stereotactic frame is used for individual treatments.
  - dose per fraction is typically larger than that is standard treatment because of complexities of radiosurgical treatments. Typical dose/fractionation regimens are: 6x7 Gy (total dose: 42 Gy) with treatment given every second day, or 10x4 Gy (total dose: 40 Gy) with treatment given daily.

15.2.8. **Commissioning of radiosurgical equipment**

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

• 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 a 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 a 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:

  (1) The *basic quality assurance protocols* covering the performance of all equipment used for target localization, 3D treatment planning and radiosurgical dose delivery.

  (2) The *treatment quality assurance protocols* dealing with calibration and preparation of equipment immediately preceding radiosurgical treatment.

  (3) *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 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 radiations.

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. The neurosurgeons, on the other hand, have had previous favorable experience with Gamma unit radiosurgery and expressed serious concerns about the mechanical stability of isocentric linacs when used in radiosurgery.

An unstable linac isocenter could adversely affect the accuracy of dose delivery and result in substandard treatments in comparison to 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 isocenter sphere (on the order of 1 mm diameter) making 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 Gamma units are superior to any linac-based radiosurgical techniques. During the past decade this consensus 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 that aim 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 robotic arm, Section 15.2.5.)

The accuracy of target localization achieved with these new frameless techniques approaches that attainable with invasive stereotactic frames. The 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**

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 cobalt-60 gamma 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 whole body except for a few specific organs which are partially or fully shielded from the prescribed dose.

15.3.1. **Clinical TBI categories**

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

1. **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).

2. **Low dose TBI** with dose delivery in 10 to 15 fractions of 10 to 15 cGy each.

3. **Half body irradiation** with a dose of 8 Gy delivered to the upper or lower half body in a single session.

4. **Total nodal irradiation** with a typical nodal dose of 40 Gy delivered in 20 fractions.

15.3.2. **Diseases treated with TBI**

Total body irradiation is used primarily as part of a preparatory cyto reductive conditioning regimen prior to bone marrow transplantation (BMT). The source of marrow may be the patient (autologous transplant), identical twin (syngeneic transplant), or histocompatible 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 the 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 the BMT, referred to as graft versus host disease. Thus, an optimal application of TBI is a very important component of a successful BMT procedure.

Most notable diseases treated with BMT are:

1. various leukemias (acute nonlymphoblastic; acute lymphoblastic; chronic myelogenous)
2. malignant lymphoma
3. aplastic anemia
15.3.3. Technical aspects of TBI

All contemporary TBI techniques use megavoltage photon beams produced either by cobalt-60 teletherapy units or linear accelerators:

- The beams are either stationary with field sizes on the order of $70 \times 200 \, cm^2$ 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 installments and switching the patient position between the two installments.

15.3.4. TBI techniques

TBI treatment techniques are carried out either with dedicated irradiators or, more commonly, with modified conventional megavoltage radiotherapy equipment. Currently, four methods are in use to administer TBI with modified conventional radiotherapy equipment:

1. Treatment at extended SSDs.
2. Treatment at standard SSDs after cobalt-60 machine collimator is removed.
3. Treatment with a translational beam.
4. Treatment with a sweeping beam.

The first two techniques use large stationary beams and a stationary patient, while the latter two use moving beams produced by translating the 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 midpoint on the level of umbilicus). The TBI procedure must deliver the prescribed dose to the dose prescription point and should maintain the dose throughout the body within $\pm 10\%$ of the prescription point dose. Uniformity of dose is achieved with the use of bolus or compensators.

15.3.6. Commissioning of TBI 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 and beam profiles (off-axis ratios). However, 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 phantoms and ionisation chambers that are used in measurement of dosimetric parameters. In contrast to standard radiotherapy, in TBI the phantoms are generally smaller than the actual field size and also smaller than the patient. This causes different scattering conditions that might adversely affect the beam output as well as percentage depth doses required in the determination of treatment times or monitor units to achieve the prescribed tumour dose.

• The accuracy of the TBI dosimetric data might be adversely affected by the relatively large portion of the ionisation chamber cable irradiated with the large TBI field as well as by chamber leakage currents and saturation characteristics which become more problematic at the relatively low dose rates used in the TBI.

15.3.7. Test of TBI 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 TBI

TBI is a complex treatment modality requiring careful treatment planning, accurate localization of organs that are to receive a reduced dose or be shielded completely from the radiation beam, and strict adherence to quality assurance protocols. These protocols fall into three categories: (1) Basic quality assurance, (2) Pre-treatment quality assurance, and (3) Treatment quality assurance.

(1) *Basic quality assurance* protocols cover the performance of 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 geometry of other critical organs, and a treatment planning system which is used for determination of lung dose.

(2) *Pre-treatment quality assurance* protocols deals with calibration and 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 into the appropriate position as well as ensuring proper functioning of any special dosimetric equipment which will be used for measuring the delivered dose to the prescription point or determining transmission of radiation through the lung.

(3) *Treatment quality assurance* protocols deal with the measurement of 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.
FIG. 15.4. Stationary beam total body irradiation techniques: (a) two short SSD parallel-opposed beams; (b) dedicated cobalt unit; (c) extended SSD – patient standing; (d) extended SSD – patient on stretcher.

FIG. 15.5. A cobalt-60 teletherapy unit dedicated for total body irradiation. The source-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.
FIG. 15.6. Moving beam total body irradiation techniques: (a) translational beam – patient moves translationally through a stationary beam; (b) sweeping beam – the beam sweeps over a stationary patient.

FIG. 15.7. A patient treated with the sweeping beam total body irradiation technique on a 4 MV linear accelerator.
15.4. TOTAL SKIN ELECTRON IRRADIATION (TSEI)

Total skin electron irradiation (TSEI) is a special radiotherapeutic technique which aims to irradiate the patient's whole skin with the prescribed irradiation dose while sparing all other organs from any appreciable radiation dose. Since skin is a superficial organ, the choice of electron beams for treatment of generalized skin malignancies 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 centers. In the past, superficial x-ray machines, Van de Graaff generators, and even machines incorporating beta particle emitting sources were used for TSEI. All contemporary TSEI procedures, on the other hand, are based on electron linear accelerators that are used for conventional radiotherapy and modified for delivery of the large and uniform electron fields required for TSEI.

- The photon contamination of electron beams used in TSEI is a potential detriment to the patient. Therefore, its magnitude must 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 patient’s skin as well as some organs (such as nails and eyes) may have to be shielded to avoid treatment morbidity.

- Typical dose/fractionation regimen is: 40 Gy in 20 fractions.

15.4.1. Physical and clinical requirements for TSEI

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

1. Physical specifications of the large stationary electron field used for TSEI;

2. Physical specifications of the dose distribution resulting from the superposition of multiple stationary electron fields; and

3. Clinical specifications.

- Physical specifications of large stationary electron fields:
  - Electron field size on the order of $80 \times 200 \text{ cm}^2$.
  - Dose uniformity at $z_{\text{max}}$ in a water equivalent phantom for at least 80% of the nominal field (typically $\pm 5\%$ from dose at $z_{\text{max}}$ in phantom on the central ray).
  - Nominal SSD: 300 to 500 cm.
  - Beam energy at waveguide exit window: 6 to 10 MeV.
  - Beam energy on phantom surface: 4 to 7 MeV.
  - Dose rate on beam central ray at $z_{\text{max}}$ in water-equivalent phantom.
  - Photon contamination of the electron beam.
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- Physical specifications of the dose distribution resulting from the superposition of multiple stationary electron fields used for the clinical TSEI:
  - Dose rate at $z_{\text{max}}$ on central ray (usually on skin surface which becomes the dose prescription point).
  - Bremsstrahlung contamination dose rate at the patient's mid-separation at the level of umbilicus.

- Clinical specifications for treatment with TSEI:
  - 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 TSEI techniques

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

1. **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.

2. **Large electron field techniques** in which a standing stationary patient is treated at large SSD with a single large electron beam or a combination of large electron beams.

3. **Rotational techniques** in which the patient is standing on a rotating platform in a large electron field.

*FIG. 15.8. Patient treated with the rotational total skin electron irradiation technique.*
15.4.3. Selection of TSEI 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 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 be treated either 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 $z_{\text{max}}$ in a tissue-equivalent phantom.

- Often the beam output as well as flatness is monitored directly on-line with two ionisation 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 umbilicus (dose prescription point) that usually is 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 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 TSEI procedure

- Based on current TSEI standards, the TSEI technique, newly introduced into a clinic, will use a large and uniform stationary electron field and 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.

- 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.
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- The basic dosimetric parameters of the large TSEI electron field are:
  - Field flatness measured at $z_{\text{max}}$ in a tissue equivalent phantom and normalized to 100 at the dose calibration point.
  - Electron beam output at the dose calibration point.
  - Percentage depth doses ($PDD$s) measured to a depth of 15 cm in a tissue-equivalent phantom.

- The $PDD$s 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 TL 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 TSEI dose distributions

In addition to the basic cylindrical dosimetry phantom, the 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 also be evaluated, underdosed skin areas identified, and boost irradiation methods 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 TSEI

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:

1. Basic quality assurance protocol dealing with the equipment used in total skin electron irradiation,

2. Pre-treatment quality assurance protocol dealing with the calibration and preparation of equipment immediately prior to TSEI treatment,

3. 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)

Intraoperative radiation therapy (IORT) is a special radiotherapeutic technique which delivers in a single session a radiation dose on the order of 10 Gy to 20 Gy to a surgically exposed internal organ, tumour, or tumour bed. Thus, the IORT combines two conventional modalities of cancer treatment: surgery and radiation therapy, 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 the IORT is applied as part of a treatment protocol that includes other modalities such as chemotherapy and external beam radiation therapy. 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 of 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 IORT

- 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 location in which the treatment unit is to be installed are selected, an applicator system must be chosen. Applicators are important for three reasons:
  
  1. to define the target area.
  2. to shield tissues outside the target area from radiation.
  3. to keep sensitive tissues from falling into the target area during irradiation.

15.5.2. IORT radiation modalities and techniques

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

1. Orthovoltage x rays.
2. Megavoltage electron beams.
3. HDR iridium-192 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 programs today are based on electron beams produced by megavoltage linacs, since electrons provide several advantages over x rays for purposes of the IORT:

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

### 15.5.3. Commissioning an IORT program

- 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 equipment, the commissioning of the IORT procedure must be carried out:
  - Radiation beam parameters must be measured and dosimetry data summarized so that it may be quickly understood and readily used. Dosimetry measurements which may be necessary, depending upon the IORT modality used, include: absolute dose output at the end of treatment applicators; central axis depth dose data; 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 practiced 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 IORT

Quality assurance of IORT treatments is in some respects even more important than that for standard radiotherapy, since the IORT treatments are almost always given in a single session, making it essentially impossible to correct a misadministration of dose.

The quality assurance in IORT consists of three components:

1. **Basic quality assurance** dealing with all IORT equipment.
2. **Pre-treatment quality assurance** dealing with equipment preparation and verification immediately prior to IORT treatment.
3. **Treatment quality assurance** during the IORT dose delivery to the patient.
15.6. **ENOCAVITARY RECTAL IRRADIATION**

In recent years increasing efforts have been directed toward the development of organ-saving therapeutic approaches for malignant neoplasms that 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 abdomino-perineal resection.

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

15.6.1. **Physical and clinical requirements for endorectal irradiation**

The main physical requirements for the technique to be successful is that the x-ray beam have a low effective energy, giving a percentage depth dose in tissue with 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 source-surface treatment distance.

Selection criteria for endocavitary rectal irradiation are as follows:

1. biopsy-proven well or moderately well differentiated rectal adenocarcinoma,
2. mobile lesion with a maximum diameter of 3 cm,
3. location of lesion within 10 cm from the anal canal, and
4. no evidence of lymph node or distant metastases.

Two techniques have been used for endorectal treatments:

1. **Short SSD technique** with SSD on the order of 4 cm and the x-ray tube inserted into the proctoscopic cone;
2. **Long SSD technique** with SSD on 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** that, in honor 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 (geographic miss of 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:
  - X-ray tube can be connected to the ~20 cm long proctoscopic cone externally, allowing the use of smaller diameter cones.
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- 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.

- Dose uniformity over the tumour volume is improved since a change in SSD of a few mm on an irregular tumour surface affects the surface dose uniformity much more at an SSD of 4 cm than 20 cm.

15.6.2. Endorectal treatment technique

The endorectal treatment technique consists of the following steps:

(1) Patient is positioned onto the proctoscopic couch and the proctoscopic cone with a plunger is inserted into the rectum.

(2) Plunger is removed, a proctoscopic viewing device is attached to the cone, and the cone is placed over the tumour.

(3a) In the short SSD technique the x-ray tube is then inserted into the cone, and both the cone as well as the x-ray tube are handheld for the duration of treatment.

(3b) 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.

(4) X-ray machine is turned on and the prescribed target dose delivered.

The total tumour dose is on the order of 80 Gy delivered in two or three fractions of 20 Gy to 30 Gy in each fraction. The fractions are typically 2 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:

(1) Basic quality assurance dealing with 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 ionisation 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.

(2) Pre-treatment 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.

(3) 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 planning target volume (PTV) while at the same time keeping the dose to specified organs at risk at doses below their tolerance dose. The conformal radiotherapy chain is based on 3D target localization, 3-D treatment planning, and 3-D dose delivery techniques:

- **Target localization** is achieved through anatomical and functional imaging: computed tomography (CT), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), positron-emission computed tomography (PET), and ultrasound (US).

- **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 multileaf collimators (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 isocenter. MLCs projecting leaf widths of less than 5 mm at the isocenter are referred to as microMLCs. 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.

- Each leaf is individually motorized and computer-controlled, allowing positioning with accuracy better than 1 mm and generation of irregular radiation fields, shaped to conform to the beam’s eye view target cross-section.

- Separate, miniature DC motor drives each leaf independently.

- Positional control and verification for the leaves is achieved by a sophisticated servo-mechanism using electronic or optical/video techniques to sense the position.
15.7.3. Acceptance testing of MLCs

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**: motion of leaves and their maximum travel; abutting of leaves on and off the central field axis; alignment of MLC axes with axes of the linac secondary collimators; positional reproducibility of leaves; interlocks for leaf and jaw positional tolerances.

- **Radiation**: transmission of leaves, leakage between leaves; leakage in junction of two abutting leaves both on field axis and off field axis; leaf penumbra both along the leaf and perpendicularly to it.

- **Software**: verification of: (i) field shaper; (ii) linkage between treatment planning system and the MLC; (iii) accuracy of field shaping and functioning of the controller.
15.7.4. Commissioning of MLCs

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, percentage depth dose, etc.

- The in-phantom dosimetric parameters, such as the relative dose factor, scatter factor, percent depth dose, tissue-maximum ratio are determined by the field shape created by the MLC collimator.

- The in-air dosimetric parameter, the collimator factor, is determined by the square or rectangular field shaped by the secondary linac collimator jaws and is considered essentially independent of MLC shaping.

15.7.5. Quality assurance program for MLCs

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

15.7.6. Intensity Modulated Radiation Therapy (IMRT)

In addition to field shaping in 2D conformal radiotherapy where the radiation fields are irregularly-shaped but of uniform intensity, an MLC may also be used to achieve beam intensity modulation for use in 3D conformal radiotherapy. From an obscure, highly specialized radiotherapeutic technique practiced in only a few specialized centers around the world, intensity modulated radiotherapy (IMRT) has developed into a mainstream radiotherapeutic technique already available in most major radiotherapy centers 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). It relies on inverse treatment planning (ITP) for determination of required intensity modulated beam maps and on 3-D multi-modality 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:

- Complexity of equipment used for dose delivery,
- Complexity of the ITP process, and
- 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,
- adjusting 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 effect among four areas that only then became well established:

1. 3-D medical imaging by CT, MRI, SPECT, and PET,
2. Inverse treatment planning,
3. Quality assurance techniques for verification of dose delivery,

15.7.7. Commissioning of IMRT systems

The steps involved in commissioning an IMRT system will depend to some degree on the type of inverse treatment planning (ITP) system to be used. Some ITP systems are simple modules within a standard 3-D treatment planning system 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 treatment planning system.

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 modeling, separate from a 3-D planning system. At least one manufacturer attempts to simplify the commissioning process by offering to carry out beam modeling for the customer, provided all necessary beam data is supplied.

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

1. **Step-and-shoot**
2. **Sliding window**
3. **Intensity-modulated arc therapy**
In the step-and-shoot mode each MLC-shaped sub-field can be set prior to the beam turning on and there is no MLC motion while the beam is turned on.

A more elegant technique, known as sliding window, has all sub-fields set while the beam is turned on.

Recently, a new delivery method called intensity modulated arc therapy (IMAT) has 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 linear accelerator hardware.

Each method of delivery needs to be commissioned separately as MLC and linear accelerator performance is stressed differently depending on the method. IMRT treatments require tighter tolerances on MLC performance than is 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 need to be developed. These tests must be able to verify the accuracy and reproducibility of MLC positioning and movement for each delivery technique that is 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 done using the standard dosimetry tools (radiographic or radiochromic film, TLD, ionisation 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 IMRT systems

A comprehensive quality assurance (QA) program must be developed to ensure accurate IMRT dose delivery. This program 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. Because of the added stress on MLC components, particularly the motors, it is a good idea to augment the standard spare parts kit to include at least several additional motors.
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15.7.9. Dose verification for IMRT 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 a patient. Actual dose delivery can then be compared to the plan and evaluated for accuracy. Several manufacturers have recently developed software and hardware which 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 RADIATION THERAPY

Over the past decade, there have been substantial advancements in the technology used to plan and deliver precision radiation therapy. Inverse treatment planning and virtual simulation aided by fusion of multi-modality images (CT, MR, and PET) of patient anatomies have revolutionized the planning of radiation therapy treatments. The efficacy of treatment delivery has also been improved with the recent introductions of intensity modulated radiation therapy (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. Inter-fraction target movement relative to reference landmarks coupled with setup 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 benefit of the more precise treatment delivery techniques.

Recently, it has become possible to image the patient anatomy just before the delivery of a fraction of radiation therapy, thus gaining precise knowledge of the location of the target volume on a daily basis. This technique is known as Image-Guided Radiation Therapy, 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 images at the time of each fraction of radiation therapy. The system must be fast and simple so as not to affect patient throughput, and be accurate within the limits of target definition and the ability to deliver a conformal dose.

Five Image-Guided Radiation Therapy systems are currently commercially available. All systems allow pre-treatment imaging immediately after a patient is positioned on the treatment couch for therapy:

- The BAT and ExacTrac systems are based on ultrasound scanning and are used in conjunction with isocentric linacs.
- The CT Primatom system is based on computed tomography (CT) imaging of patient anatomy and is used in conjunction with isocentric linacs.
The tomotherapy system is based on megavoltage CT imaging (MVCT) and used in conjunction with a miniature linac mounted on a CT-type gantry.

The CyberKnife system is based on on-line paired orthogonal planar x ray imagers used in conjunction with a patient CT data set and a miniature linac mounted onto a robotic arm.

15.8.1. The BAT system

Nomos Corporation (USA) introduced the BAT system in the mid 1990s with BAT representing the acronym for “B-Mode Acquisition and Targeting”. The system is comprised of a cart-based ultrasound unit positioned next to a linac treatment couch and is used by a radiation therapist to image a target volume prior to each fraction of a patient's radiation therapy. The relationship of the target volume to a reference point, usually the linac isocenter, is determined interactively by the user and compared to the target volume originally contoured in the CT dataset. Suggestions for patient translation to get the target volume into the same position relative to isocenter as in the treatment plan are made by the system. The therapist can then move the patient based on this information, resulting in a more accurate dose delivery.

The BAT system has found its greatest application in pelvic radiation therapy, particularly for prostate cancer. It is well known that the prostate can move significantly from one day to another within the pelvis relative to bony anatomy. Imaging the prostate target volume trans-abdominally 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.

15.8.2. The ExacTrac ultrasonic module

BrainLab (Germany) has also developed an ultrasound-based system for image-guided radiation therapy 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 patient position to compensate for target movement and setup inaccuracies.

15.8.3. CT Primatom

A system comprised of a linac and a CT unit at opposite ends of a standard radiation therapy treatment couch has been developed and is marketed by Siemens (Germany). This system allows precise CT imaging of patient anatomy prior to each fraction of radiation therapy. Not only can the patient be shifted to compensate for target motion and setup inaccuracies; this system can also in principle allow clinicians to account for changes in target volume size and shape over a multi-fraction course of radiation therapy.
15.8.4.  Tomotherapy

The tomotherapy concept for delivering radiation therapy 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, will be released shortly for clinical use and combining treatment planning, patient positioning, and dose delivery into one system.

In the tomotherapy system, IMRT is delivered with a linac (nominal beam energy: 4 MV, average energy: 1.36 MeV) that is mounted on a 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 couch 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 a megavoltage CT scan (MVCT) of patient anatomy at any time before, during, or after treatment. The MVCT image data is acquired with a 738-element Xenon ion chamber array that rotates on the gantry opposite the linac. This image guidance allows fine adjustment of patient 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 treatment position, allowing, at least in principle, an evaluation of the true dose distribution delivered to the patient.

15.8.5.  CyberKnife

The CyberKnife was developed in the mid 1990s by Accuray (USA) as an innovative tool for intracranial stereotactic radiosurgery (see Section 15.2.5). It delivers the dose with a miniature (10⁴ 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 toward 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 Cyber-Knife.

The location of the lesion is pre-determined through a family of axial CT-images that serves as a base for determination of a set of 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 on-line orthogonal pair of digital x-ray imagers, a patient CT data set fused with MR and/or PET images and a miniature linear accelerator 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 spatial accuracy, the CyberKnife also offers several other advantages over the 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 lung and prostate using surgically implanted fiducial markers as a reference frame, and
- Capability for on-line tracking of target motion. This results either from patient motion during treatment or from organ motion within the patient during treatment.

15.9. RESPIRATORY GATED RADIATION THERAPY

In the current radiation therapy 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 normal tissue complication probability (NTCP) results in smaller margins around the tumour and a need to deal effectively with organ motion during the treatment.

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) that is a special accessory added to a linac to compensate automatically and instantly for the effects of respiratory movement on external beam radiation therapy to the chest and upper abdomen.

Respiratory gated treatment has been 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 the real-time position management RGS and 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 Intensity Modulated Radiotherapy (IMRT) and other 3D conformal treatments.

A reflective marker is placed on the patient’s chest and a video camera tracks its up and down movement. The continuous signal is processed by a computer that initiates a beam-hold in the linac, when the breath movement exceeds parameters determined during the treatment simulation. The target motion is correlated with the motion of external markers in stimulation. These markers are then used in treatment to control appropriate beam-on times to limit treatment to those time periods where 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. Breathing volume is measured by the machine’s mouth-piece 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.

15.10. PET/CT SCANNERS AND PET/CT 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 (positron emission tomography) and CT (computed tomography) have been used as imaging modalities since the early 1970s. Below are some characteristics of each individual unit demonstrating the rationale behind the development of the combined PET/CT scanner:

- CT scanner was invented by G. Hounsfield and A. Cormack and is based on an acquisition of a large number of cone beam projections around a patient acquired by a detector array and representing transmission measurements of x rays through a patient. The measured transmission data are reconstructed to produce a tomographic image, most commonly through the filtered back-projection 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 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 for tumours it detects.

- PET has always provided information on the metabolic function of organs or tissues by detecting how cells process certain compounds such as, for example, glucose. Cancer cells metabolize glucose at a much higher rate than normal tissues. By detecting increased radio-labeled glucose metabolism with a high degree of sensitivity, PET identifies cancerous cells, even at an early stage when other imaging modalities may miss them. However, because of its relatively poor resolution, PET cannot pinpoint the exact size and location of tumours to a precision required for optimal diagnosis and treatment planning. This limitation until recently precluded a wider use of PET machines in radiotherapy.

- In a PET study, one administers a positron-emitting isotope by injection or inhalation. The radioactive isotope circulates through the bloodstream to reach a particular organ. The positrons emitted by the radioisotope have a very short range in tissue and undergo annihilation with an available electron. This process generally results in an emission of two gamma rays, each with energy of 0.511 MeV, moving away from the point of production in nearly opposite directions (at 180° to each other).
The PET machine generates transverse images depicting the distribution of positron-emitting radioisotopes 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 back-projection.

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

The radioisotopes used in PET studies are produced by bombardment of an appropriate stable isotope with protons from a cyclotron (see Section 5.4) thereby producing positron-emitting radioisotopes that are subsequently attached to clinically useful biological markers. The common positron-emitting radioisotopes used in PET imaging studies are listed in Table 15.1. The fluorine-18 radioisotope attached to fluorodeoxyglucose (FDG) is the biological marker most commonly used in studies involving glucose metabolism in cancer diagnosis and treatment.

The relatively short half-life of the positron-emitting isotopes 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. On the other hand, 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.

TABLE 15.1. COMMON POSITRON-EMITTING RADIOISOTOPES USED IN PET

<table>
<thead>
<tr>
<th>Radioisotope</th>
<th>Symbol</th>
<th>Half-life (min)</th>
<th>Maximum positron energy (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-11</td>
<td>C-11</td>
<td>20.5</td>
<td>960</td>
</tr>
<tr>
<td>Nitrogen-13</td>
<td>N-13</td>
<td>10</td>
<td>1200</td>
</tr>
<tr>
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BIBLIOGRAPHY


