CHAPTER 1

INTRODUCTION

1.1 CANCER

The World Health Organization (WHO) defines cancer as the rapid proliferation of abnormal cells that grow beyond their normal boundaries and can affect any part of the body as well as spread to other parts. According to a survey conducted in 2008, cancer was the leading cause of mortality globally, accounting for 7.6 million deaths, or 13 percent of the total. Lungs, prostate, stomach, liver, breast, cervix, etc. are the most prevalent locations of cancer, with lungs being the most common (1.37 million). It is estimated that there will be around 13.1 million cancer deaths by 2030 (WHO, 2013).

Cancer can be decreased or controlled mostly by early detection and appropriate treatment programmes, often known as cancer therapy. The goal of cancer therapy is to eradicate the malignancy and prevent it from spreading. The therapy consists of four distinct procedures that can be used separately or in combination. These are *surgery*, which removes the mass of the tumor, *chemotherapy*, which uses drugs to slow and stop the growth of the tumor, *immunotherapy*, which uses the immune system of the body to change the immune response, and *radiotherapy*, which uses ionising radiation to treat the cancer. The stages of tumor development and mechanism of metastasis are presented in Figure 1.1.

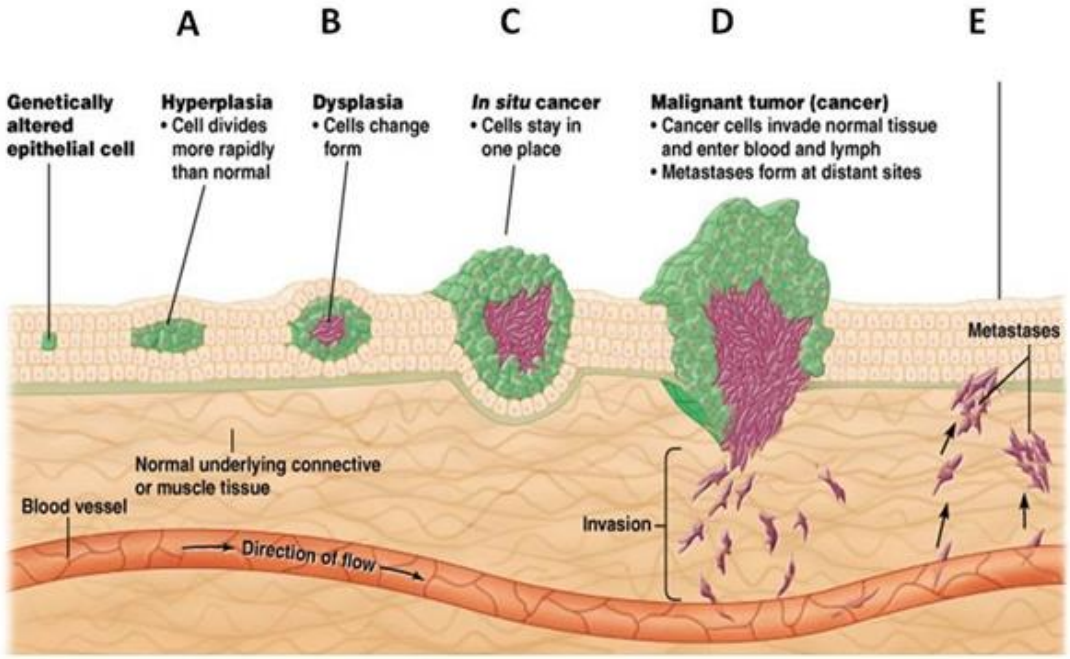

Figure 1.1: Stages of tumor development and mechanism of metastasis (https://tel.archives-ouvertes.fr/tel-00912341/)

1.2 RADIOTHERAPY

Radiotherapy is one of the prime modality in the treatment of cancers. It uses indirectly ionizing radiation such as photons and gamma rays, or directly ionizing charged particles such as electrons, heavy ions etc., to cause damage to the malignant and non-malignant cells. It may also be used as an adjuvant treatment in combination with surgery and chemotherapy. Two major categories for the application of radiation for cancer treatment are brachytherapy and external beam therapy (EBRT) (Holsti, 1995). The brachytherapy is a type of radiation therapy used to treat cancer, involving the placement of a radioactive material such as Radium-226, Cobalt-60, and Iridium-192 etc., either temporarily or permanently, directly inside the tumour or adjacent to the tumor. For external-beam treatment, the patient lies underneath a machine that emits radiation or generates a beam of x-rays (Figure 1.2). This technique is also called teletherapy, or long distance treatment (Karzmark, 1973). The source of radiation is X-ray or photons from medical linear accelerator (LINAC), or a radioisotope that emits high-energy gamma rays.

During the first 20 years after the discovery of X-rays in 1895, radiotherapy treatment was administered using prototype X-ray units (Lederman, 1981; Thwaites and Tuohy, 2006). The machines were often unshielded, resulting in over exposure to scattered radiation of patients and staff in the treatment room. These machines were suitable only for the treatment of superficial lesions like skin. In 1920s “deep” therapy machines of energies 120 – 300 kV began to be developed for treating lesions well below the skin (Karzmark, 1973; Lederman, 1981; Thwaites and Tuohy, 2006; Podgorsak, 2005). These units used adjustable levers to swivel the X–ray tube to position so that patients could be treated from different directions. X-rays generated in the 10–30 kV range are known as grenz rays, whereas the energy range for superficial therapy, contact therapy, and orthovoltage therapy, and super voltage therapy units is about 30–50 kV, 50–150 kV, 150–500 kV, and 500–1,000 kV, respectively (Thwaites and Tuohy, 2006; Podgorsak, 2005).

However, demand for higher energy units were felt to treat deep-seated tumors. The invention of the ^{60}Co teletherapy unit by H.E. Johns in Canada in the early 1950s provided a tremendous boost in the quest for higher photon energies and placed the cobalt unit at the forefront of radiotherapy for a number of years (Thwaites and Tuohy, 2006). The advantages of higher energy X-ray beams had been recognized

from the some of the drawbacks of cobalt therapy beams include the need for source replacement approximately every 4 to 5 years, poor field flatness for large fields and large penumbra, and lower depth dose, which can be overcome with high energy photons generated by LINAC.

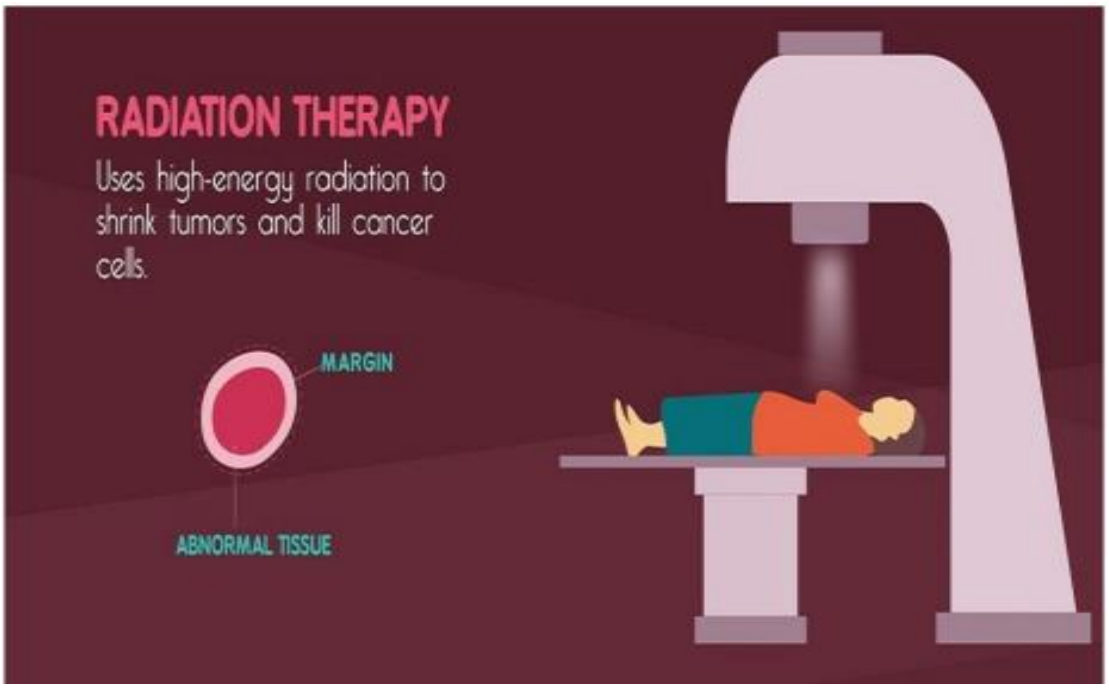

Figure 1.2: External beam radiation therapy
(https://breastcare-surgeon.com/radiation-therapy.html/)

1.3 MEDICAL LINEAR ACCELERATOR

The LINAC is a device that uses high frequency microwaves to accelerate electrons generated by electron gun to high energies through an accelerator tube (Podgorsak, 2005; Cho, 2018). These electrons are allowed to strike a high atomic number (Z) target for production of high energy x-rays. In general, such LINAC produce electron beams of energies between 4 to 25 Mega-electron Volts (MeV) and photon beams of nominal energies 6 Mega Volt (MV), 10 MV and 15 MV. The modern LINACs are usually mounted isocentrically and the operational systems are distributed over five major and distinct sections of the machine (Figure 1.3);

- Gantry: A frame housing the treatment head, electronic portal imaging device (EPID), and KV imaging system in a LINAC.
- Gantry stand or support

- Modulator cabinet
- Patient support assembly (i.e. treatment couch)
- Control console

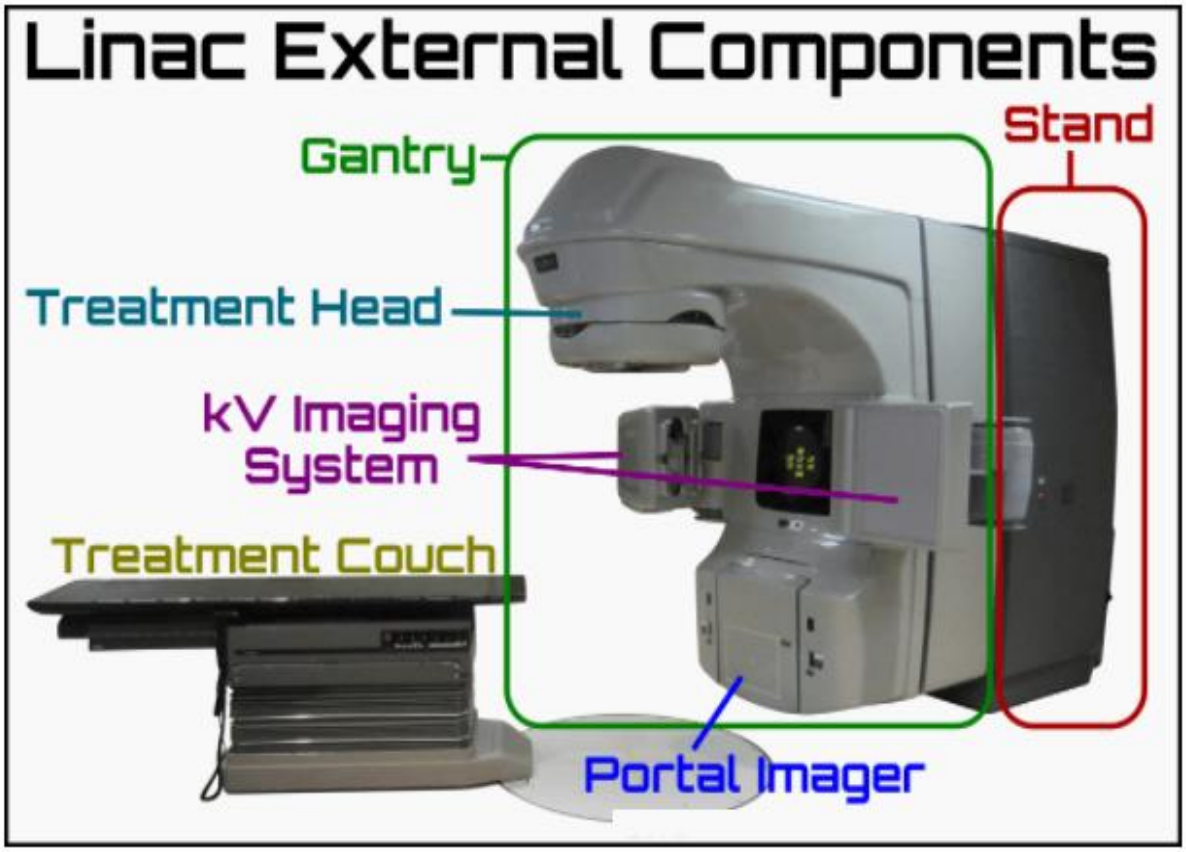

Figure 1.3: Components of a medical linear accelerator (https://oncologymedicalphysics.com/)

The main beam forming components of a modern medical LINACs are usually grouped into six classes (Figure 1.4):

- Injection system
- Radiofrequency (RF) power generation system
- Accelerating waveguide
- Auxiliary system
- Beam transport system
- Beam collimation and beam monitoring system

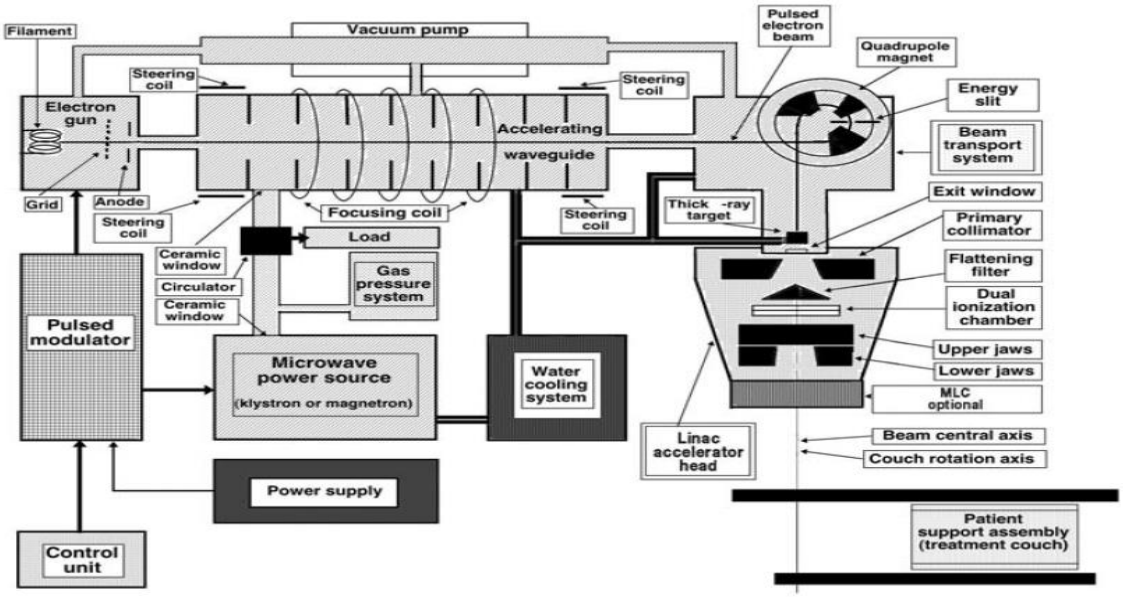

Figure 1.4: A schematic diagram of medical linear accelerator (http://www-naweb.iaea.org/)

1.3.1 Electron Gun

Two types of electron gun are in use as sources of electrons in medical LINACs, diode type and triode type. Both electron gun types contain a heated filament cathode and a perforated grounded anode, in addition, the triode electron gun also incorporates a grid. Electrons are thermionically emitted from the heated cathode, focused into a pencil beam by a curved focusing electrode and accelerated towards the perforated anode through which they drift to enter the accelerating waveguide.

1.3.2 RF power generation system

The microwave radiation used in the accelerating waveguide to accelerate electrons to the desired kinetic energy is produced by the RF power generation system, which consists of two major components: an RF power source and a pulsed modulator. The RF power source is either a magnetron or a klystron. Both are devices that use electron acceleration and deceleration in a vacuum for the production of high power RF fields. Both types use a thermionic emission of electrons from a heated cathode

and accelerate the electrons towards an anode in a pulsed electrostatic field; however, their design principles are completely different.

1.3.3 Accelerating waveguide

Waveguides are evacuated or gas filled metallic structures of rectangular or circular cross-section used in the transmission of microwaves. Hollow single tube is not useful for accelerating electron, so the coupling cavities are used to divide into sections with central holes, in order to couple and distribute microwave power between adjacent cavities and to provide a suitable electric field pattern for the acceleration of electrons. Steering coil ensures electrons travel longitudinal axis. Circulator is placed between Klystron & Accelerator; it prevents or stops the reflected waves coming from the accelerator structure. The accelerating waveguide is evacuated to allow free propagation of electrons. Two types of accelerating waveguide have been developed for the acceleration of electrons

- Travelling waveguide.
- Standing waveguide.

In travelling waveguide, microwaves enter the accelerating waveguide on the gun side & propagate towards high energy end of the waveguide, where they are absorbed. In the standing waveguide, each end of the accelerating waveguide is terminated with a conducting disc to reflect the microwave power, resulting in a buildup of standing waves in the waveguide.

1.3.4 Auxiliary system

The LINAC auxiliary system consists of several services that are not directly involved with electron acceleration, yet make the acceleration possible and the LINAC viable for clinical operation. The LINAC auxiliary system comprises four systems:

- A vacuum pumping system producing a vacuum pressure of ~10–6 torr in the accelerating guide and the RF generator.
- A water cooling system used for cooling the accelerating guide, target, circulator and RF generator.

- An optional air pressure system for pneumatic movement of the target and other beam shaping components.
- Shielding against leakage radiation.

1.3.5 Electron beam transport

In low energy LINACs the target is embedded in the accelerating waveguide and no beam transport between the accelerating waveguide and target is required. Bending magnets are used in LINACs operating at energies above 6 MeV, where the accelerating waveguides are too long for straight-through mounting (Podgorsak, 2005). The accelerating waveguide is usually mounted parallel to the gantry rotation axis and the electron beam must be bent to make it strike the X ray target or be able to exit through the beam exit window. Three systems for electron bending have been developed: 90º bending; 270º bending (achromatic); 112.5º (slalom) bending (Figure 1.5).

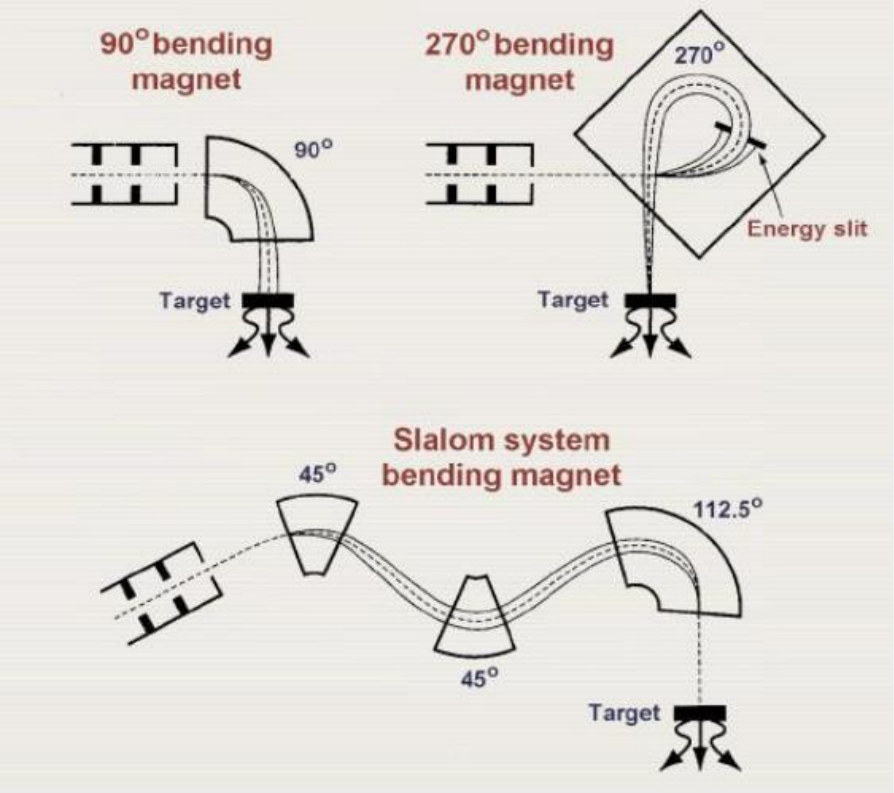

Figure 1.5: Schematic diagram of three systems for electron beam bending (http://www-naweb.iaea.org/)

1.3.6 LINAC treatment head

The LINAC head contains several components that influence the production, shaping, localizing and monitoring of the clinical photon and electron beams. Electrons originating in the electron gun are accelerated in the accelerating waveguide to the desired kinetic energy and then brought, in the form of a pencil beam, through the beam transport system into the LINAC treatment head, where the clinical photon and electron beams are produced. The important components found in a typical head of a fourth or fifth generation LINAC include:

- **Retractable X-ray targets:** Clinical photon beams are produced with a target–flattening filter combination.
- **Primary collimator:** The primary collimator defines a maximum circular field for a radiation beam.
- **Flattening filters and electron scattering foils:** The flattening filters and scattering foils are mounted on a rotating carousel or sliding drawer for ease of mechanical positioning into the beam, as required for different energies.
- **Dual transmission ionization chambers:** The dose monitor chambers are located between the flattening filter or scattering foil and the photon beam secondary collimator. Dual transmission ionization chambers are used for monitoring the photon and electron radiation beam output as well as the radial and transverse beam flatnesss (Greene, 1986).
- **Secondary collimators:** These are adjustable rectangular collimator consisting of two upper and two lower independent jaws and producing rectangular and square fields with a maximum dimension of 40 × 40 cm2 at the LINAC isocentre.
- **Field light and optical distance indicator:** The field light illuminates an area that coincides with the radiation treatment field on the patient's skin, while the optical distance indicator is used to place the patient at the correct treatment distance by projecting a centimetre scale whose image on the patient's skin indicates the vertical distance from the LINAC isocentre.

1.4 FF AND FFF PHOTON BEAMS

This LINAC is used to treat varieties of cancer cases utilizing electron as well as photon beams. The conventional LINAC uses a conically shaped flattening filter (FF) made up of a high Z material in the photon beam delivery mode and acts as an attenuator, the beam hardener and the scatterer. It is located between the primary collimator and the monitor chamber and its main role is to compensate the non-uniformity of photon beam dose variation across the radiation field. However, it may not be necessary for the certain type of advanced radiotherapy treatments. The advanced beam therapy techniques such as stereotactic radio surgery/radiotherapy (SRS/SRT) and stereotactic body radiotherapy (SBRT) where inhomogeneous dose distributions are applied and intensity modulated radiotherapy (IMRT) where varying fluence pattern across the beam are delivered, have stimulated the increasing interest in operating standard LINAC in a flattening filter free (FFF) mode (Georg et al., 2011).

A standard LINAC can therefore be used for generating photon beams either with FF or without FF. As shown in Figure 1.6, the conically shaped FF made of a high Z material is located in the gantry of the LINAC, between the primary collimator and the monitor chamber, and its main function is to flatten the output dose so that it has a uniform beam profile at the reference depth. Besides the beam uniformity, some disadvantages of FF for advanced radiotherapy techniques are that it acts as an attenuator, reduces dose rate, and is a major cause of relatively more head scattering from the LINAC head (Georg et al., 2011; Vassiliev et al., 2006). The removal of FF from the path of X-ray beam results in 2-4 times increase in dose rate, inhomogeneous beam profile and a decrease in head scattering, which reduces leakage and out-of-field dose (Ponisch et al., 2006; Cashmore, 2008; Parsai et al., 2007; Kragl et al., 2009; Dalaryd et al., 2010; Sharma, 2011; Zhang et al., 2015; Ting, 2012; Wang et al., 2010; Mancosu et al., 2012; O'Brien et al., 1991). The higher dose rates and therefore a shorter delivery time of FFF beam would keep the patient on the treatment couch for a shorter period of time. Thus, giving more comfort to the patient and decreasing the chances of intra-fractional setup inaccuracies (O'Brien et al., 1991). These are critical elements in the techniques used for treatment of small lesion such as SRT, SBRT and SRS because of the usage of high fraction doses and of small margins for planned

target volume (PTV), thus requiring very high accuracy and precision. A number of theoretical and experimental studies related to the clinical implementation of unflat photon beams demonstrated their suitability and superiority over flat photon beams (Georg et al., 2011; Vassiliev et al., 2006; Ponisch et al., 2006; Cashmore, 2008; Parsai et al., 2007; Kragl et al., 2009; Dalaryd et al., 2010; Sharma, 2011). Therefore, this study aimed to evaluate the dosimetric, treatment planning and pre-treatment verification aspects of FFF beams in order to increase the available data on this topic. The rescaling of the FFF beam profile to a FF beam is shown in Figure 1.7 as suggested by Pönisch et al.

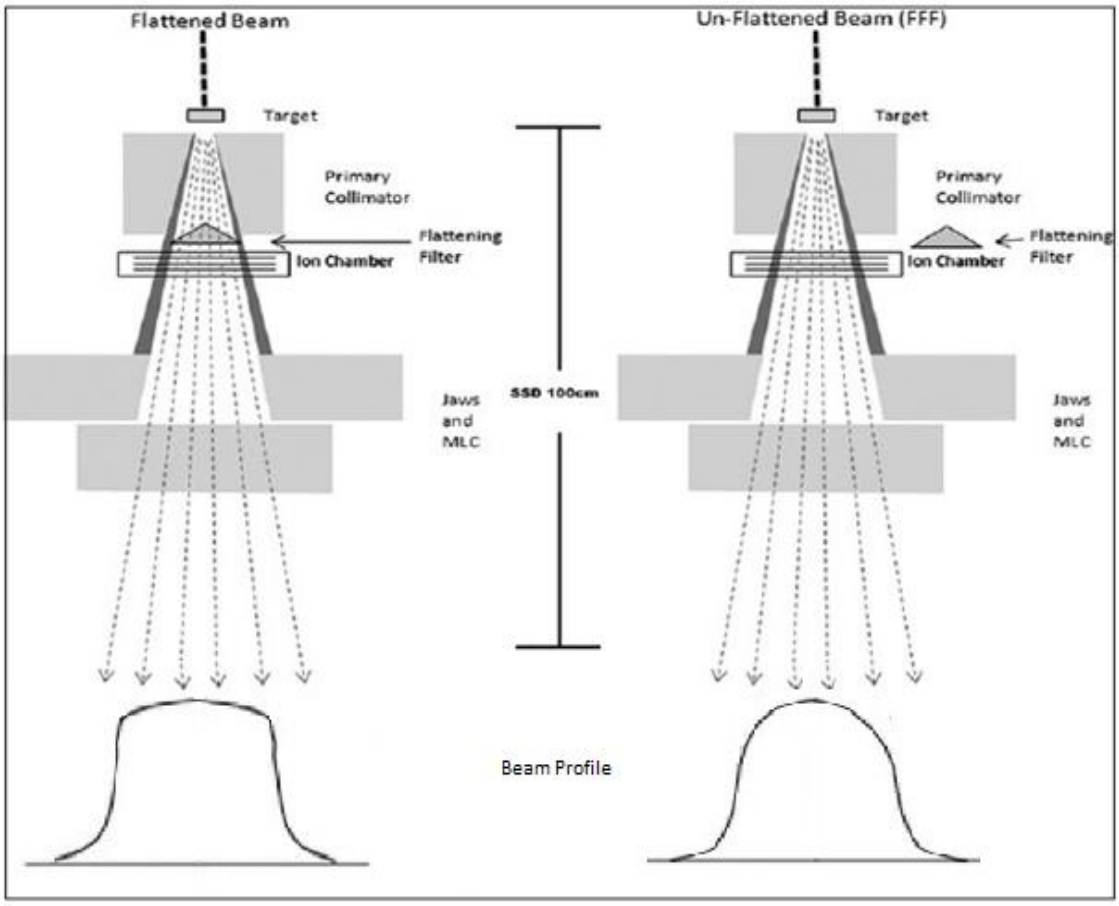

Figure 1.6: Schematic diagram of FF and FFF photon beam modes in a medical LINAC

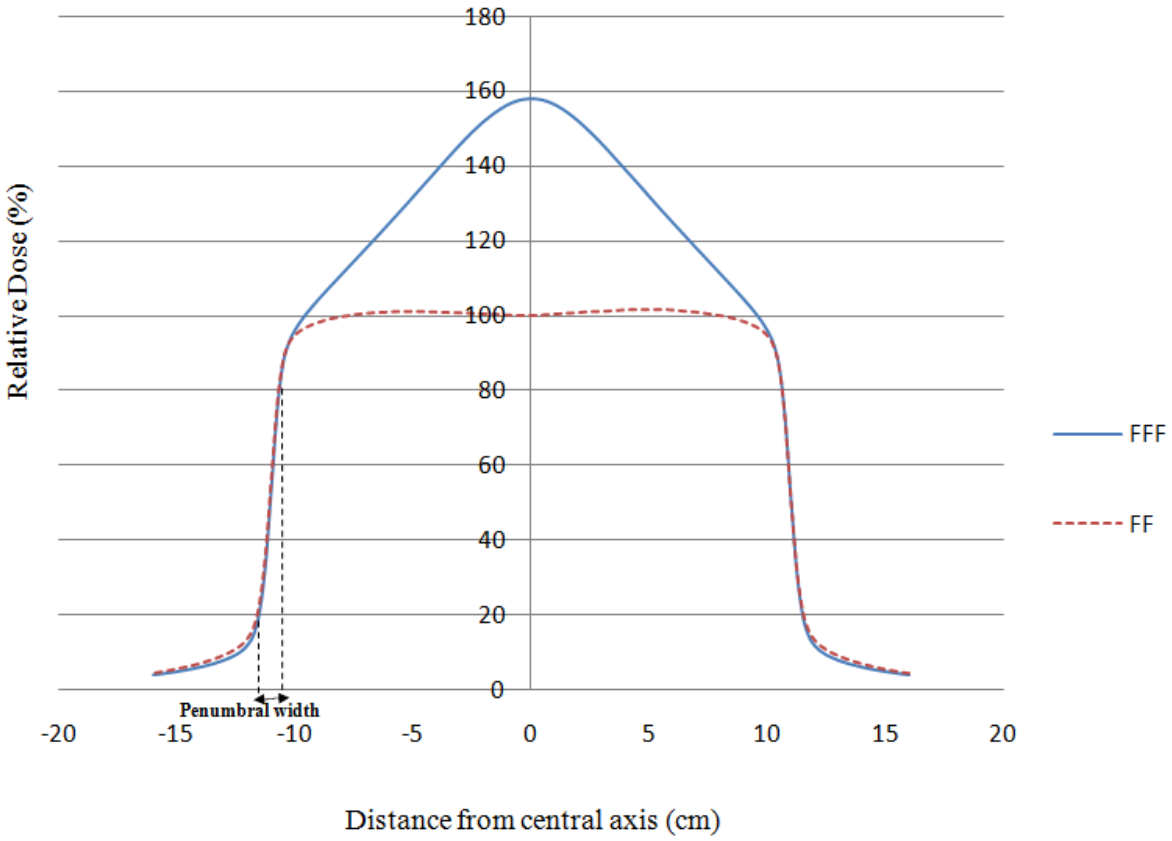

Figure 1.7: Schematic description of (i) rescaling of FFF beam profile with FF beam as suggested by Pönisch *et al*. (ii) and penumbra of FFF beam

1.4.1 Brief History of FF & FFF Beams

The FFs have been considered as an integral part of the treatment head of a LINAC for more than 50 years and reasons for the longstanding use are, however, historical ones (Georg et al., 2011). In the 1991, O'Brien et al studied 6 MV FFF photon beams and main interest of the study was the need to reduce radiosurgery treatment delivery time. Several other studies were performed after this and were mainly motivated with research interest in the characteristics of FFF beam (Sixel and Faddegon, 1995; Zefkili, 1994; Zhu and Bjarngard, 1995; Karlsson and Zackrisson, 1997). In 2004, Fu et al investigated the effect of removing the flattening filter on reducing IMRT delivery time in a treatment planning study.

In 2006 onwards, MD Anderson and other groups began publishing. Their outcomes suggest that with a FFF accelerator better radiation treatments can be

developed, with shorter treatment times and lesser doses to healthy tissues (Georg et al., 2011; Vassiliev et al., 2006; Ponisch et al., 2006; Cashmore, 2008; Parsai et al., 2007; Kragl et al., 2009; Dalaryd et al., 2010; Sharma, 2011; Zhang et al., 2015; Ting, 2012; Wang et al., 2010; Mancosu et al., 2012; O'Brien et al., 1991; Sixel and Faddegon, 1995; Zefkili, 1994). In 2010, Varian Medical Systems developed LINAC (TrueBeam) equipped with both FF and FFF photon beams and the product was made available for commercial uses from then onwards.

The development of an FFF beam mode in the LINAC is thought to provide additional benefits to SBRT (Mancosu et al., 2012; O'Brien et al., 1991; Sixel and Faddegon, 1995; Zefkili, 1994; Zhu and Bjarngard, 1995; Karlsson and Zackrisson, 1997; Fu et al., 2004; Palmans et al., 2017; Tanny et al., 2015; Azangwe et al., 2014; Huq et al., 2018; Tyler et al., 2016; Underwood et al., 2015). During 2010 to 2021, hundreds of medical linear accelerators with FFF features have been installed worldwide (Bigle et al., 2010; Chen et al., 2010; Ong et al., 2010; Hong et al., 2010; Holt et al., 2011; Rana, 2014; Yan et al., 2017; Hoffmann et al, 2018; Tajaldeen et al., 2019; Shiraishi et al., 2019; Pokhrel et al., 2020).

The primary advantage of FFF beam is the ability to use much higher dose rates, which results in a shorter delivery time (Georg et al., 2011). Shortening the delivery time would keep the patient on the treatment table for a shorter period of time. As a result, it provides more comfort to the patient and also reduces the chances of inaccuracy due to movement of the patient. Because of the use of high fraction doses and small tumor margins, these are critical elements in SBRT to provide very high precision in treatment delivery (Sharma, 2011; Zhang et al., 2015; Ting, 2012; Wang et al., 2010). With these advantages in mind, many researchers are still working to establish the general guidelines regarding the acceptance, commissioning, quality assurance, planning and pre-treatment verification of FFF photon beam so that it becomes a full replacement to the FF photon beam.

1.4.2 Challenges associated with FFF Beams

The flattening filter free beam mode is a relatively new technology, so there are still some uncertainties that need to be clarified before it becomes a full replacement to the flattened beam option. Some of the research gaps such as establishing new technical

criteria, standards and definitions regarding the FFF beam, similar as they exist for the conventional beam (Lederman, 1981; Cashmore, 2008). Also the selection of appropriate detectors for commissioning and periodic quality assurance of small FFF beams.

The application of FFF beam requires further development of the today's MLC technology because for many optimized segments in static IMRT the travelling time of the leaf is too long and for dynamic and rotational IMRT, the speed of the leaf collimators is slower than required (Cashmore, 2008). Moreover, the limitation is more evident for large treatment fields. When such fields are in use, MLCs are used to regulate the central high intensity of the beam, for example supplying a more uniformed dose within the large planning target volume (PTV). Providing beam uniformity would also lead to a reduction in the initial dose rate, which actually was one of the main advantages of the FFF beam (Kragl et al., 2009).

This means that FFF beam delivery is more efficient in lesions of relatively small size (Parsai et al., 2007; Kragl et al., 2009; Dalaryd et al., 2010). Advanced radiotherapy treatment of small lesions needs faster treatment delivery and rapid dose fall off in the area surrounding the tumor, which requires the use of FFF photon beams. However, because FFF mode is a relatively new technology, multiple studies on this topic have been published, the majority of which use FF photon beams (Sharma, 2011; Zhang et al., 2015; Ting, 2012; Wang et al., 2010).

Therefore, more research on FFF beams is needed to increase the amount of data available on this topic. Also more information is needed when it comes to the immediate and long term biological effects of the very high dose rates on the healthy tissues and the ones inside the target volume (Parsai et al., 2007; Kragl et al., 2009). In addition, all dosimetric properties and beam modeling, beam data acquisition and absolute dosimetry of the beam have to be carefully studied especially when it comes to small field applications (Kragl et al., 2009). Lastly, some other uncertainties that need to be clarified are related to the higher dose rates and the performance of the radiation detectors, starting from the ion chambers to the pre-treatment verification devices.

1.5 SMALL FIELD DOSIMETRY AND DETECTORS

Since the development of advanced techniques like IMRT, VMAT, SBRT, SRT, and SRS, it has become necessary to use relatively small fields that are either dynamic or static. Because of the higher dose rate, FFF photon beams are often preferred in these advanced radiotherapy techniques, particularly in SRS, SRT, and SBRT, where small radiation fields with high fraction doses are employed to treat tumours. Small FFF photon beams deliver the dose quickly and precisely to the tumor. This reduces inter- and intra-fractional setup errors and spares nearby healthy tissues.

In the field of radiation dosimetry, a clear definition of a small field has not yet been agreed upon. When the field dimensions are smaller than the lateral range of the secondary charged particles and there is partial occlusion of the primary beam source by the collimating device, a photon beam is frequently defined as having a small field. The dosimetry of small fields presents a number of challenges that standard photon dosimetry does not. Some of these are as follows:

- Partial occlusion of direct photon beam source
- Drop in output and overlapping penumbrae
- Steep dose gradient
- Lateral electron disequilibrium (depending on beam energy and irradiating medium)
- Volume averaging effect
- Widening of full width half maxima (FWHM) of the dose profile
- Problem in dosimetric measurement (detector size and construction)
- Detector becomes too large to resolve the penumbra and perturbs fluencies at the position of measurement
- Beam alignment
- Selection of detector and the analysis of its response

Because of these challenges, it is more challenging to choose a detector that will accurately measure small fields than it is for standard or large fields. The large and small field scenarios are shown in Figure 1.8. The desirable detector characteristics for small field dosimetry include high spatial resolution, low noise, low energy dependence, low directional dependence, water equivalence, high stability, and clinical usability. Clearly, there is no standard dosimeter for small fields, as no

detector possesses all of the aforementioned characteristics. Some of the most common types of dosimeters used in small fields are ionisation chambers, films, TLDs, polymer gels, metal oxide semiconductor field effect transistors (MOSFETs), diamond detectors, silicon diodes, alanine dosimeters, and Monte Carlo (MC) simulations.

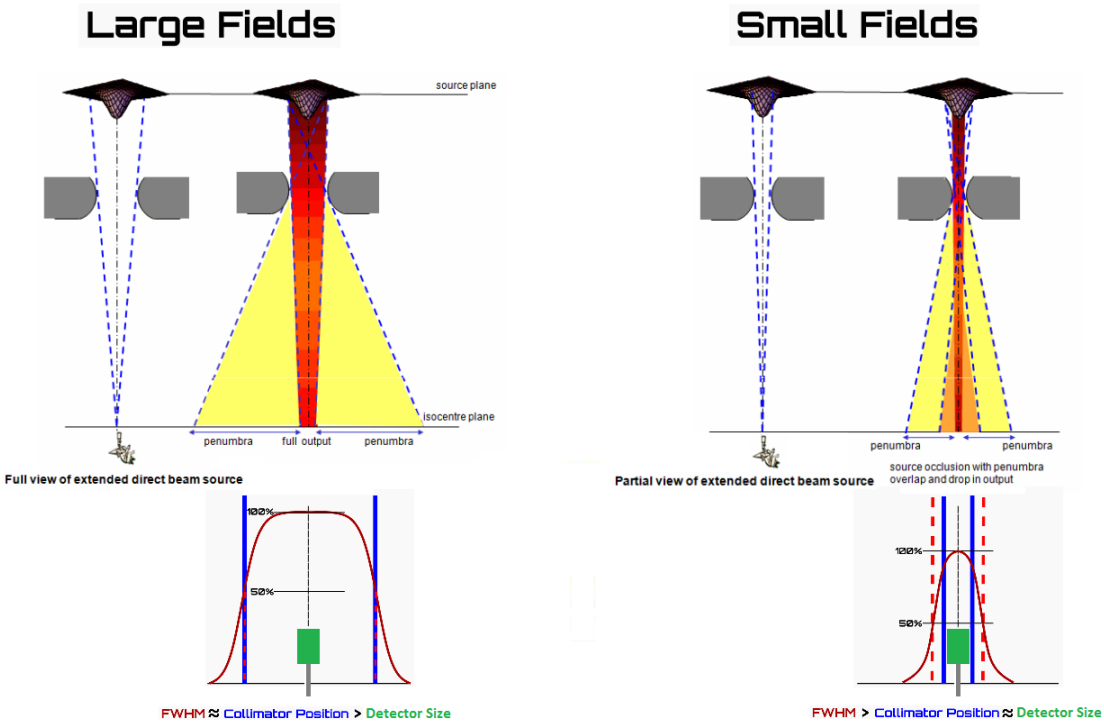

Figure 1.8: A schematic illustration of the large and small field scenarios.

1.5.1 Ionization Chambers

Ionization chambers are sometimes limited to small-field measurements. The detector size and lack of lateral charged particle equilibrium (LCPE) are the limiting constraints in employing ionisation chambers. Small-size vented air-filled ionisation chambers, also known as micro chambers or pinpoint chambers, exhibit good water equivalence in the kV energy range and their MV energy dependence can be rectified using beam quality correction factor (kQ) values obtained from literature or the manufacturer. The pinpoint is a type of ion chamber with a very small active volume (< 0.1 cm^3) that is intended specifically for evaluating relative beam profiles in small photon fields. This chamber must be calibrated against a Farmer chamber in order to

measure absolute dose. Because of their limited sensitivity volume, these detectors do not exhibit stem or polarity effects. Because of volume averaging, the pinpoint underestimates output factors in very small fields. When employed in axial orientation, with the chamber axis towards the focus, the spatial resolution of these chambers can reach 2 mm. When measuring cross-beam profiles in the penumbra area, a lack of LCPE is an issue.

1.5.2 Semiconductor detector

- **Diode detectors:** The p-type of silicon diode is ideal for radiotherapy dosimetry because it is less likely to be damaged by radiation and has a much lower dark current. In silicon diodes, it takes 3.6 eV of energy to make a pair of electrons and holes. This is much less energy than is needed to make a pair of ions in air, so diodes are more sensitive than ionisation chambers. Because of their great sensitivity per volume, diodes can be made in small sizes. Diodes are often used in small-field dosimetry because they can be read in real time, have good spatial resolution, and are small.

- **Diamond detectors:** Diamond detectors function as solid-state ionisation chambers. Their sensitive volume is made of natural diamond. They are water equivalent due to the similarity of carbon's atomic number to tissue. They have a size and spatial resolution similar to typical silicon diode detectors. There are also other benefits, such as high dose response, directional independence, low leakage current, and high resistance to damage from radiation.

- **Metal oxide–silicon semiconductor field-effect transistor:** MOSFETs are sandwich-type devices with a p-type silicon semiconductor substrate on one side and a metal gate on the other side of an oxide layer that keeps the two from touching. They are extensively used for small field dosimetry due to their small active area and direct reading ability, as opposed to some dosimeters, such as TLDs, which require pre and post processing. MOSFETs are energy independent in the megavoltage range. Furthermore, these dosimeters are dose rate independent.

1.5.3 Thermoluminescent dosimeter

TLDs used in radiation dosimetry are made of LiF crystal, which has an effective atomic number of 8.3 and is similar to water or tissue. When the LiF crystal is heated, the measured intensity of light emitted from the crystal is related to the absorbed dose. The basic requirements of a TLD are good reproducibility, low hygroscopicity, and high sensitivity for very low dose measurements or good response at high doses in radiotherapy and mixed radiation fields. TLDs are a promising way to measure the absorbed dose in a small field because of their high spatial resolution and dose response. TLDs are relative dosimeters and must therefore be calibrated against absolute dosimetry systems such as a calibrated ion chamber. A ^{60}Co gamma source is commonly used. Due to their small size, TLDs are useful for measuring dose-distribution in medicine and biology.

1.5.4 Film dosimetry

Film dosimetry is appealing due to its high spatial resolution, wide accessibility, and flexibility in placing the film in humanoid phantoms. Also, the short measuring time and the fact that film dosimeters are good detectors for measuring dose distribution in two dimensions. These detectors are classified into two types: radiographic and radiochromic film. The radiographic film requires processing conditions, and the densitometer used to read the dose influences the radiographic film response. The advantage of radiochromic films over radiographic films is that they are self-developed and do not require any chemical processing to obtain an image of the radiation dose distribution. Furthermore, these films are not affected by ambient light and do not require processing in a darkroom.

1.5.5 Plastic scintillation detector

Plastic scintillation detectors, often known as PSDs, have a number of desirable qualities, some of which are water equivalence, high spatial resolution, independence from energy and dosage rate, and linear dose response. The most significant drawback

associated with dosimetry with PSD-based devices is the production of Cherenkov radiation. This light is produced when an optical fibre is placed within the radiation field. It is recommended that the light be removed from the primary signal in order to remedy this shortcoming. Recent years have seen the use of PSDs in more contemporary forms of radiation therapy, such as IMRT and SRS.

1.6 RADIOTHERAPY PLANNING

External radiotherapy has undergone numerous developments since it was first used about 70 years ago (Benedict et al., 2010). Throughout the years, a variety of treatment techniques have been employed depending on the available technology. However, only a few of them—the most recent ones—will be covered here: 3DCRT, IMRT, and VMAT are all treatment techniques that can be used for SBRT. Before discussing each technique in greater detail, it will be useful to explain a few definitions of clinical structures.

1.6.1 Clinical structures

The goal of radiotherapy is to deliver a high dose of radiation to the tumour while sparing the surrounding normal tissues as much as possible. As a result, external photon beam is performed by employing multiple beams at various angles. The volume definition of the involved structures within the patient's body is an important factor in an effective curative treatment. SBRT, just like conventional radiation therapy, uses the ICRU 50 and 62 definitions (Figure 1.9) for gross tumour volume (GTV), clinical target volume (CTV), internal target volume (ITV), planned target volume (PTV), and organ at risk (OAR).

- GTV is the gross visible location of the tumour, including its extensions. GTV can be practically defined by utilising any of the imaging modalities: CT, MRI, ultrasound, or a combination of any of them.
- CTV includes the GTV and other nearby sub-clinical malignant diseases that are to be eliminated. In most cases, it is defined as the GTV plus a margin

(usually between 0.5 cm and 1 cm) around the GTV, but in a few cases, it can be the same volume as the GTV.

- ITV is defined as the CTV plus an additional internal margin to compensate for internal physiologic movement and variations in size, shape, and position of the CTV.
- PTV is defined as the ITV surrounded by an adequate margin to account for geometrical uncertainties in treatment delivery, as well as machine and patient set-up uncertainties.
- OARs are healthy organs near the PTV whose irradiation may influence treatment planning and/or prescribed dose.

In this thesis, only PTV and GTV are used because ITV and CTV are defined in clinical cases. Therefore, they are not applicable to the phantom study and are also not commonly used structures in SBRT.

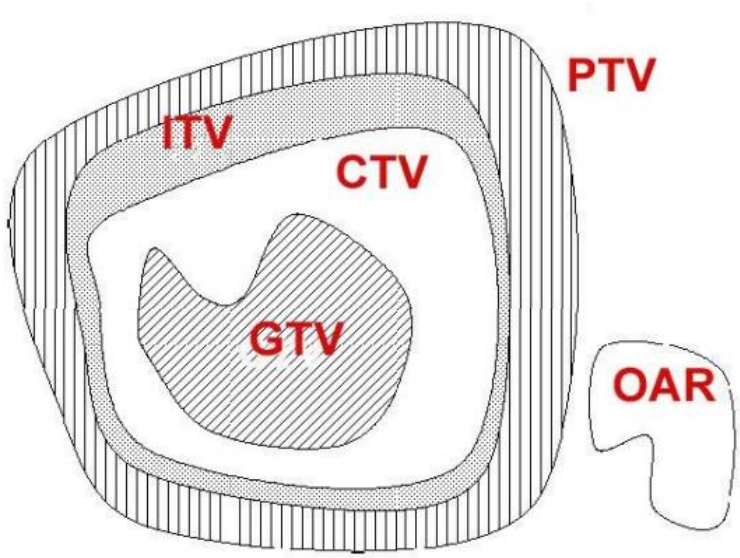

Figure 1.9: Schematic presentation of clinical structure definition as per ICRU 50 and ICRU 62.

1.6.2 3DCRT

Three-dimensional conformal radiation therapy, or 3DCRT, is an advanced technique that uses imaging technologies to generate three-dimensional images of a patient's tumour and surrounding organs and tissues. The key difference between 3DCRT and other conventional radiation therapy modalities is the use of three-dimensional images

in the treatment planning process. A patient's treatment team can generate a highly specialised plan to deliver a precise radiation dose to a tumour using this thorough information. As a result, cancerous cells can receive a higher and more efficient dose of radiation. At the same time, the radiation exposure to nearby healthy tissues can be significantly reduced.

If 3DCRT is suggested for a patient, three-dimensional images of the tumour and surrounding structures are generated using any of the imaging modalities: CT, MRI, positron emission tomography (PET), or a combination of any of them. Following that, the structures and targets are delineated. The fields and beams required for treatment are then designed. In this case, the optimization problem necessitates constantly modifying several parameters using a trial-and-error method or experience until the desired conformity is achieved. These are the number of fields, their aperture, beam weights, directions, and beam modifiers (bolus, compensators, and wedges). Multiple fields are used to avoid using very high energy beams and to spread the dose over a larger volume. However, creating more than four fields poses the issue of beam modifiers' production (Khan, 2012).

1.6.3 IMRT

IMRT is without a doubt the ultimate tool in external beam radiation therapy and is considered more advanced than 3DCRT (Williams, 2000; Taylor et al., 2004). However, it should be noted that technical precision in dose planning and delivery alone does not guarantee superior clinical results. PTV design, organ localization, patient immobilisation, and online portal imaging are all equally important. In short, the success of IMRT when indicated is determined not by whether it is used but by how it is used. The user instructs the software to use mathematical algorithms to find the best possible plan. The user can assign a dose to a 3D volume enclosing the PTV. The user can assign maximum doses to 3D volumes for critical structures. It is possible to obtain concave-shaped isodose distributions. 3DCRT is a forward planning, while IMRT is an inverse planning (Figure 1.10).

- Forward planning: Specify Beams weights, wedge angles, beam modifiers. User has direct control over these parameters at any point in the treatment planning process. From field definition to dose distribution. Dose delivery with uniform radiation intensity.

- Inverse planning: User does not specify these parameters. The numbers, energy & direction of the beams are still chosen by the planner. But once beams have been specified, the computer takes complete control over all parameters e.g. MUs, weights, beam modifiers etc.

In IMRT, intensity-modulated beams are directed at the PTV from various angles. Multi leaf collimators (MLCs) are used to modulate beam intensity by segmenting each treatment field and applying a discrete dose to each segment (Ezzell et al., 2003). Inverse planning software is used to optimise the intensity of each beam in order to meet the prescribed dose distribution criteria for the composite plan. The inverse planning optimization iteratively minimises the difference between the desired and realised dose distributions. The two most common delivery methods of IMRT are static MLC and dynamic MLC.

- In Static MLC delivery, several different MLC-shaped fields (segments) are generated for each beam orientation. Summing all the segments results in modulated field intensity. Because the radiation beam is only turned on when the segments are in place, this method is known as step-and-shoots IMRT or static IMRT delivery (Siochi et al., 1999).

- In dynamic MLC delivery, the beam is kept on during field shaping, which is not the case in static MLC. It is only turned off when the beam's angle changes. The intensity pattern is formed by moving the leaf pairs across the field at a predetermined velocity pattern. The sliding window technique is another name for dynamic MLC.

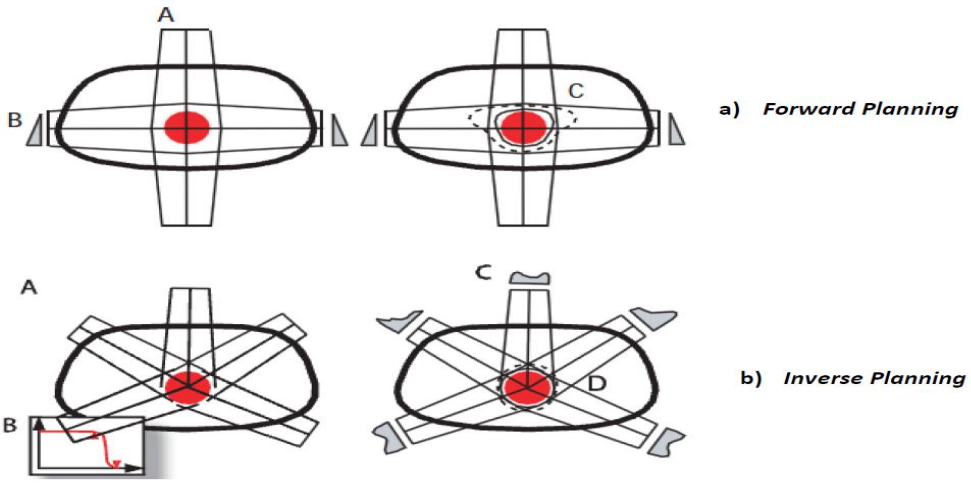

Figure 1.10: A schematic representation of (a) forward planning, and (b) inverse planning (Eclipse reference guide, Varian Medical Systems, 2010)

1.6.4 VMAT

VMAT is a more advanced form of IMRT in which a single or multiple radiation beams sweep in continuous arcs around the patient, reducing both treatment time and patient dose. IMRT is performed at a few specific angles depending on the number of therapy beams, whereas VMAT applies IMRT at all angles of the rotation arc around the patient. VMAT is considered to be a more effective delivery method than IMRT, and its treatment plans are as good as or better than IMRT ones. When compared to conventional treatment methods, the typical treatment time for VMAT is shorter. The radiation beam remains on while the gantry rotates around the patient, and the desired dose distribution is achieved by varying the dose rate, gantry speed, and MLC speed, which are all computer controlled parameters. The sequence of control points is executed quickly, each of which defines the MLC shape, MLC segment dose, and a gantry-angle window across which each shape sweeps dynamically (Craft et al., 2012). Shorter delivery times reduce the risk of target motion and make patient treatment more comfortable (Videtic et al., 2019; Ding et al., 2013). A schematic representation of IMRT and VMAT delivery is shown in Figure 1.11. The examples of arc geometries for VMAT planning are shown in Figure 1.12.

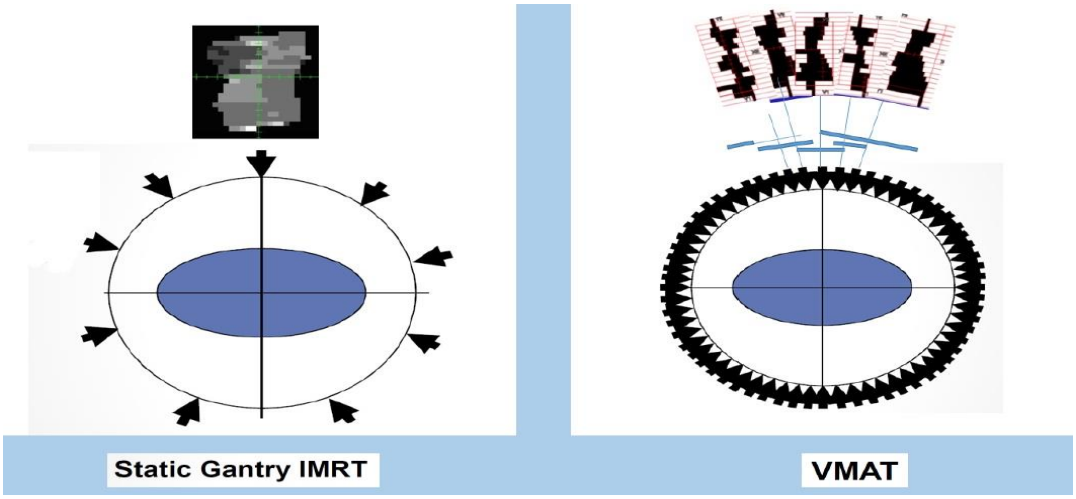

Figure 1.11: A schematic representation of IMRT and VMAT delivery (https://indico.ictp.it/event/a14234/session/7/contribution/42/material/slides/0.pdf/)

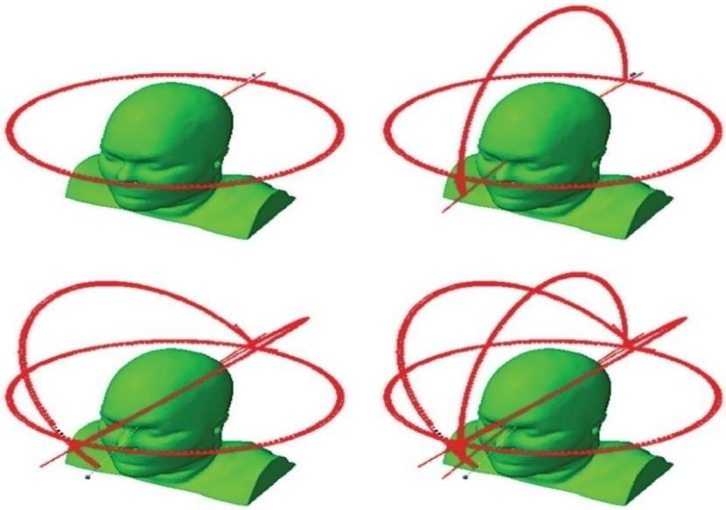

Figure 1.12: Examples of arc geometries for one, two, three, or four arc VMAT plans for cranial SRS planning. **(**doi: 10.1016/j.prro.2011.12.003)

1.6.5 SBRT

SBRT is a technique that accurately delivers very high doses of radiation to an extracranial target in one or a few treatment fractions using multiple co-planar and non-coplanar beams directed by a set of coordinates, resulting in a high biological effective dose (BED). Stereotactic treatment was first introduced in Sweden in 1992, following the development of an extracranial stereotactic frame for treating chest and

abdomen tumours (Ponisch et al., 2006). Since then, the technique has improved and gained popularity as a result of its advantages over conventional treatments. SBRT is extremely effective in treating early stage primary and oligometastatic cancers in the abdominal, pelvic, and thoracic cavities, as well as the spinal and paraspinal cavities. The conformation of high doses to the target and rapid fall-off doses away from the target is critical for minimising normal tissue toxicity.

SBRT requires a precise target definition, target motion management, delineation of a relatively tight PTV, conformal treatment planning, set up verification using image guidance throughout the treatment, and dose verification QA prior to each treatment (Timmerman et al., 2011). SBRT is more convenient for patients and potentially more cost-effective than conventional radiation therapy due to the limited number of treatment fractions. Furthermore, when compared to conventional treatments, SBRT has a greater number of treatment fields. SBRT can be performed using 3DCRT, IMRT, a combination of the two, or the VMAT technique, depending on the treatment case. Beams can also be co-planar or non-coplanar, FF or FFF (Benedict et al., 2010). When it comes to dose delivery time, the choice of these options becomes critical. Long delivery times are frequently problematic for patients who are unable to stay in one fixed position due to pains or medical issues (Holt et al., 2011). As a result, FFF beam based VMAT SBRT techniques are thought to provide the best solution. The steps of radiotherapy treatment planning (Figure 1.13) are as follows:

- **Patient selection criteria:** The majority of patients treated with SBRT are those with lung (Primary or Oligomet), liver, and spinal tumour and Prostate with a maximum cross-sectional diameter of up to 5 cm. However, the diameter value varies from hospital to hospital and it can get also up to 7 cm in few cases (Benedict et al., 2010).
- **Immobilization:** Stereotactic body frames immobilise the patient physically while also providing an initial approximate target localization that is refined by in-room image-guided techniques. The current image-guided positioning systems reduce the need for proper immobilisation but do not eliminate it. Vacuum cushions, a localizer arch that can be attached to the body frame or the LINAC couch top, and abdominal compression to reduce respiratory motion are all options.

- **Simulation imaging:** SBRT treatment requires precise delineation of the patient's anatomy, planning targets, and clear imaging for localization. The main imaging technique used in SBRT is CT, which is useful in locating pulmonary nodules, parenchyma diseases, and chest-wall involvement for superior sulcus tumours and lung disease. MRI is being used more frequently in SBRT applications such as prostate, spinal, chest, and solid abdominal tumours. Compared to CT, PET greatly improves diagnosis and staging in terms of specificity and sensitivity.
- **Patient simulation:** It should include the target as well as all organs at risk in order to acquire geometric and dosimetric information for treatment. A normal scan length should be 5-10 cm above and inferior to the treatment field borders. For non-coplanar treatment procedures, the scan length may be extended by 15 cm inferior/superior beyond the target borders. CT slice thickness of 1–3 mm is recommended for most clinical cases.
- **Treatment planning:** SBRT plans can be generated using a variety of beam arrangements, such as fixed fields, conformal arcs, and IMRT or VMAT. The plans can be generated through forward or inverse planning based on dose constraints. A multiple number of beams or uninterrupted arcs are frequently used to ensure target coverage, fast dose falloff away from the target, and normal tissue dose sparing within acceptable limits.

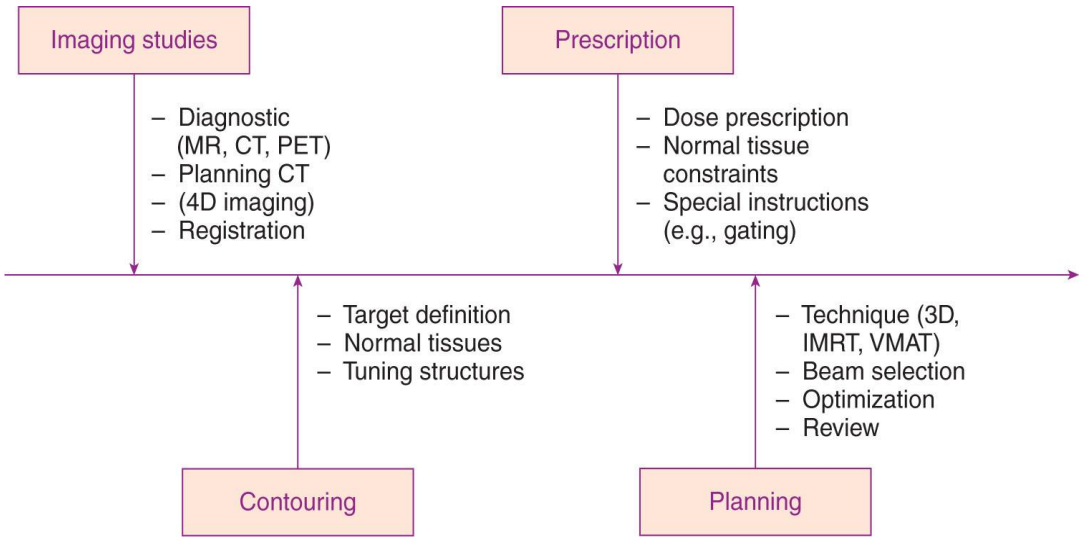

Figure 1.13: Steps of radiotherapy treatment planning

1.7 TREATMENT PLANNING SYSTEM

TPS is used in external beam radiotherapy to generate beam shapes and dose distributions with the goal of maximising tumour control while minimising normal tissue complications. 3D models of patient anatomy and tumour targets can be created in TPS for treatment planning. The entire treatment planning process involves many steps, and the medical physicist is responsible for the overall integrity of the computerised TPS to accurately and reliably produce dose distributions and associated calculations for external beam radiotherapy. TPS now offers plan optimizations that take biological aspects into account, as well as many additional tools to make treatment planning as precise and user-friendly as possible (Eclipse reference guide, Varian Medical Systems, 2010).

The first treatment planning systems were analogue one and dedicated to calculating the 2D dose distribution. The "Wheatley Integrator," the first such computer, was reported in New York, with isodose distribution represented by a matrix of numbers stored on punch cards. Then, in the 1960s, a digital computer was developed to generate several depth dose tables and isodose charts. TPS evolved into a more robust, faster, accurate and user-friendly tool as technology advanced. Improvements in treatment planning hardware and software have been most noticeable in the graphics, calculation, and optimization aspects of current systems. Modern TPS can display beam's eye views (BEVs) of radiation beams and digitally reconstructed radiographs (DRRs) for arbitrary dose distributions. Dose calculations algorithms have progressed from simple 2-D models through 3-D models to 3-D Monte Carlo techniques, and increased computing power continues to improve calculation speed. Some of the most recent dose calculation algorithms used in the Eclipse treatment planning system (TPS) are discussed below;

1.7.1 Analytical Anisotropic Algorithm

The AAA algorithm, which is used in the Eclipse treatment planning system, is a rapid and accurate approach for calculating dose in both homogeneous and non-homogeneous tissues for all photon energies utilised in the external beam therapies. The algorithm is based on a 3D pencil beam convolution-superposition algorithm that separately simulates primary photons, scattered extra-focal photons, and electron scattering. The algorithm's use of analytical convolution significantly shortens the calculation time. The AAA

algorithm configuration is mostly based on Monte-Carlo simulations, and beam modifiers (such as MLCs, wedges, compensators, and others) are incorporated into final dose calculations. The AAA method is divided into two parts: the configuration algorithm and the real-dose calculation algorithm (Eclipse algorithms reference guide, Varian Medical Systems, 2010).

1.7.2 Acuros XB algorithm

The Acuros XB algorithm was recently implemented in the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, USA) for photon dose calculation. This algorithm is classified as a Linear Boltzmann Transport Equation (LBTE) Solver. The goal of LBTE solvers, like those used in Monte Carlo techniques, is to provide exact modelling of dose deposition in medium. Monte Carlo (MC) and explicit LBTE solvers, such as Acuros XB, should yield the same end results. When comparing LBTE solvers to MC simulations, one distinguishing feature is the absence of uncertainty owing to statistical noise in the computed dose.

1.7.3 Optimization of dose distribution

Based on the method of optimization, dose optimization algorithms determine optimal or actual fluence maps that satisfy a given set of dose objectives defined by the operator during planning (i.e., beamlet or direct aperture optimization). Varian Medical System (Palo Alto, California, United States) has recently developed the photon optimization (PO) algorithm to enhance IMRT and VMAT optimizations in Eclipse TPS versions 13.5 or later. The PO algorithm combines and replaces the two old algorithms, namely the Progressive Resolution Optimizer (PRO) for volumetric modulated arc therapy (VMAT) and the Dose Volume Optimizer (DVO) for static field intensity-modulated radiotherapy (IMRT).

Both PRO and PO algorithms generate VMAT plans based on dose–volume objectives and a series of control points that determine MLC leaf locations and MU/degree as a function of gantry angle. Initial conditions are set for both PRO and

PO algorithms using control points representing each VMAT field; a multi-resolution approach and an objective function (the sum of dose–volume and user defined goals) are used to optimise the plan. The multi-resolution dose calculation (MRDC) technique is used to improve dose calculation accuracy using progressive dose calculation segments based on the objective function values using a point cloud-based model. Four multi resolution levels are traversed throughout the optimization procedure, with the number of dosage calculation segments increasing gradually at each level. The number of control points remains constant during the whole optimization procedure.

The primary difference between PO and PRO is that the PRO algorithm uses a point cloud-based model for defining structures, whereas PO algorithm uses a new volume representation in which structures, DVH computation, and dose sampling are defined spatially by using a single matrix over the image. The voxel resolution of the matrix is based on user-specified fixed values (1.25, 2.5, or 5 mm). The DVH of the structure is calculated using the volume weight of each voxel. In contrast to PRO, which generates leaf locations and MU/degree as a function of gantry angle, the MRDC method generates control point outputs and is primarily controlled by leaf sequencing.

During optimization, the desired dose-volume can be specified using either an "upper objective" or "lower objective". An upper objective specifies the maximum dose of radiation that can be delivered to a given volume of a structure. The minimal effective dose delivered to a given volume of the selected structure is established by the lower objective. The user specifies the dose and the volume in both cases. The NTO is used to apply a sharp dose gradient outside the PTV and prevent hotspots (very high dose regions) in healthy tissues.

1.8 PATIENT-SPECIFIC QA

Patient-specific QA plays an essential role in ensuring the quality of treatment for every individual patient. The primary objective of these QAs is to ensure that the intended dose distribution for a particular patient is physically verifiable and that intensity-modulated beams or arcs are technically feasible. In IMRT, MLC is used to modulate fixed static beams in a sophisticate manner across the treatment field.

VMAT is an advanced form of IMRT that delivers continuous radiation while the gantry of the linear accelerator rotates around one or more arcs, and a number of parameters are varied throughout this process, including the MLC aperture shape and orientation, gantry rotation speed, and dose rate. Due to the high complexity of IMRT and VMAT delivery, dose distribution verifications (typically in 2D) are always required. There are several options used to measure 2D dose distributions: ionization chamber arrays, diode detector array, electronic portal imaging devices (EPID), radiographic and radiochromic films.

1.9 RESEARCH OBJECTIVES

The research work has been carried out in order to achieve the following objectives:

1) Comparative study of beam profile and output doses of small unflat LINAC photon beams using ionization chambers, TLD, diode detector and radiochromic film for selection of appropriate detector for dosimetry.
2) Comparative study of different planning procedures adopted for FFF beam based stereotactic body radiotherapy (SBRT) treatment plans using Acuros and AAA algorithms for dose calculation.
3) To verify the radiation dose delivery of Unflat photon beam using Map check, Arc check and Portal dosimetry systems.