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Radiotherapy For Lung Cancer

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SUMMARY

Lung cancer affects a life-sustaining system of the body, the respiratory system. The respiratory system is accountable for one of the vital functions of life, breathing. Breathing enables one to take in oxygen and expel carbon dioxide. Every cell in the body depends on oxygen to function.

Cancer is a state caused by the uncontrolled growth of cells. There are different kinds of cancer. These kinds are named according to the type of cell that is growing in an unchecked way. Cancer can arise from nearly any part of the body. More specifically, lung cancer explicates when normal lung cells maintain genetic damage that ultimately leads to uncontrolled cell multiplication. Lung cancer cells have the ability to invade neighboring tissues and spread or metastasize to distant parts of the body. If lung cancer is left unhealed, it eventually causes death.

The great reserve capacity of normal lungs permits cancerous lung tumors to grow for years without jeopardizing lung function. The lungs do not have many nerves to impart pain messages so a cancerous lung tumor can grow for many years without causing any symptoms. This silent growth of lung cancer has led scientists to develop various methods such as lung cancer screening in the past few years. The process that gives the opportunity to define whether the cancer has spread and to what extent is called staging. As for the treatment of lung cancer, the deadly disease is currently cured by three forms of treatment. These are: surgery, chemotherapy and radiotherapy. They are used on the patient in combination or separately depending on the type of lung cancer from which he or she suffers and the stage of illness. The medical machine that enables doctors to perform the radiation therapy procedure is the medical linear accelerator (LINAC). The practice of radiotherapy requires not only excellent clinical skills but also appropriate technical expertise.
ΠΕΡΙΛΗΨΗ

Ο καρκίνος του πνεύμονα επηρεάζει ένα σύστημα διατήρησης της ζωής του σώματος, το αναπνευστικό σύστημα. Το αναπνευστικό σύστημα είναι υπεύθυνο για μία από τις ζωτικές λειτουργίες της ζωής, την αναπνοή. Η αναπνοή επιτρέπει σε κάποιον να πάρει οξυγόνο και να αποβάλει στο περιβάλλον του το διοξείδιο του άνθρακα. Η λειτουργία κάθε κυττάρου στο σώμα εξαρτάται από το οξυγόνο. Ο καρκίνος είναι μια κατάσταση που προκαλείται από την ανεξέλεγκτη ανάπτυξη των κυττάρων. Υπάρχουν διάφορα είδη καρκίνου. Αυτά τα είδη ονομάζονται ανάλογα με τον τύπο του κυττάρου που αναπτύσσεται με μη ελεγχόμενο τρόπο. Ο καρκίνος μπορεί να προκύψει από σχεδόν οποιοδήποτε μέρος του σώματος. Πιο συγκεκριμένα, ο καρκίνος του πνεύμονα εμφανίζεται όταν στα υγιή κύτταρα του πνεύμονα προκύπτει γενετική βλάβη που τελικά οδηγεί σε ανεξέλεγκτη πολλαπλασιασμό των κυττάρων. Τα κύτταρα του καρκίνου του πνεύμονα έχουν την ικανότητα να εισβάλουν στους γειτονικούς ιστούς και να εξαπλώνονται ή να κάνουν μετάσταση σε απομακρυσμένα μέρη του σώματος. Εάν ο καρκίνος του πνεύμονα παραμείνει αθεράπευτος, τελικά προκαλεί θάνατο. Η λειτουργία των φυσιολογικών πνευμόνων επιτρέπει στους καρκινικούς όγκους του πνεύμονα να αναπάντησαν για χρόνια χωρίς να διακυβεύεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου. Εάν ο καρκίνος του πνεύμονα αναπτύξει σε πολλά μέρη του σώματος, τα υγιή κύτταρα του πνεύμονα δεν ανακαλύπτονται σε στάδιο που να αντιμετωπίζεται η πνευμονική λειτουργία. Οι πνεύμονες δεν έχουν πολλά μηνύματα πόνου, μεταδίδουν μηνύματα πόνου.
ασθένειας. Η ιατρική μηχανή που επιτρέπει στους γιατρούς να εκτελέσουν τη διαδικασία της ακτινοθεραπείας είναι ο ιατρικός γραμμικός επιταχυντής (LINAC). Η πρακτική της ακτινοθεραπείας απαιτεί όχι μόνο εξαιρετικές κλινικές δεξιότητες αλλά και κατάλληλη τεχνική εμπειρογνωμοσύνη.
INTRODUCTION

Lung cancer affects a life-sustaining system of the body, the respiratory system. The respiratory system is accountable for one of the vital functions of life, breathing. Breathing enables one to take in oxygen and expel carbon dioxide. Every cell in the body depends on oxygen to function. If the supply of oxygen is aggravated in any way, the entire body is affected. The understanding of the manner in which the lungs and respiratory system operate shall enable the understanding of how lung cancer offends the body.

1.1 The Respiratory System

1.1.1 Breathing

The respiratory system includes one of the most essential functions, breathing. When one breathes in or inhales, the body receives oxygen. Oxygen is a gas in the atmosphere that is absolutely required to maintain life. When one breathes out or exhales, discards carbon dioxide from the body, a gas produced by normal body functions. Casting off carbon dioxide is indispensable because inordinate amounts of carbon dioxide are toxic. The lungs are the organ in the body where essential oxygen is taken in, and toxic carbon dioxide is released. When the lungs don’t operate properly, other organs in the human body have difficulty in operation. Thus, the health of the lungs has instant effects on the complete health of the human body.

The respiratory system is made up of those body parts that helps taking air in and expel carbon dioxide. Air comes in through either the nose or the mouth. It passes to the throat (pharynx), and is pulled into the windpipe (trachea). The trachea splits in two branches between the lungs sending one branch to each lung. These branches are called the right and left main bronchus.
Air moves in and out of the body by the action of muscles. The diaphragm is a large muscle that is placed below the lungs. It separates the lungs and other organs in the chest from the organs of the abdomen (Fig. 1). When the diaphragm shrivels or distends, it moves down causing the lungs to expand and pull in air. When the diaphragm relaxes, it moves up, pushing against the lungs and causing them to expel air, just like a pump. This movement is the result of the diaphragm and other muscles of the chest automatically contracting and unbending with each inhale and exhale.

Fig.1. The respiratory system.
1.1.2 The Lungs

The lungs take over most of the space in the chest cavity, which extends from the collarbones to the diaphragm. The top, cone shaped part of the lung that suits under the collarbone is called the apex. The bottom part of the lung which is wider and rests on the diaphragm is called the base. The right lung is normally larger than the left. It is divided into three sections or lobes, the upper (also called superior), middle, and lower (also called inferior). The left lung has two lobes, the upper and lower. The left lung has an indentation called the cardiac notch to make room for the heart. The lungs comprise elastic fibers that allow the lungs to expand and contract. The right and left main bronchi carry air in and out of the lungs. They are the beginning of a system of airways called the bronchial tree. The bronchial airway system is called a ‘tree’ for a very obvious reason. The airways are branched out approximately 20 times in the lungs. At each branch point, the airways become smaller and more numerous resembling the branches of trees. The main bronchi branches out for each lobe of the lung. From here, the airways divide into segmental bronchi, one for each lung segment. Segmental bronchi divides several times into smaller airways. The final branches of the bronchial tree are called atria. The atria end in tiny, microscopic air sacs called alveoli. Alveoli resemble clusters of grapes under the microscope. Each lung contains about 300 million alveoli. Alveoli are surrounded by tiny blood vessels called capillaries. There are about one billion capillaries in the lungs, more than three for each air sac (Fig. 2). The blood in the capillaries is separated from the air in the alveoli only by the extremely thin alveoli and capillary walls. This close proximity allows gases to be exchanged between the blood and the lungs in a process called respiration. Inhaled oxygen enters the blood from the alveoli. Carbon dioxide leaves the blood and enters the alveoli to be exhaled.
1.2 The Bond Between The Respiratory And Circulatory Systems

1.2.1 The Respiratory Cycle

The respiratory and circulatory systems have narrowly related functions. The function of these two systems is sometimes referred to together as the cardiorespiratory system.

The respiratory system is accountable for receiving oxygen and expelling carbon dioxide. Approximately, it is the circulatory system’s job to deliver the oxygen that has been taken in by the lungs to the body tissues. In addition, circulatory system picks up carbon dioxide from
the tissues and delivers it to the lungs where it is exhaled. Every cell of the body needs oxygen to perform its functions. Carbon dioxide is emitted as these functions are performed and must be eliminated to prevent exorbitant quantities from accumulating in the tissues. Uninterrupted removal of carbon dioxide from the human body is of paramount importance for health just as the continuous supply of oxygen.

In the respiratory cycle, oxygen is picked up by the capillaries surrounding the alveoli (Fig. 3).

![The cardiorespiratory system.](image)

The blood which is rich in oxygen is carried to the heart, which pumps the blood into arteries that carry it to the tissues of the body. In the tissues, capillaries release oxygen and pick up carbon dioxide. This carbon dioxide-rich blood is carried by veins back to the heart, which pumps it to the lungs. Carbon dioxide is released from the blood into the alveoli and new oxygen is picked up, beginning the cycle again. The success of the respiratory cycle is dependent on the very thin walls of the alveoli. These walls normally allow for a quick and easy exchange of oxygen and carbon dioxide (Fig. 4). Lung diseases like emphysema and cancer can damage the
thin, fine and susceptible alveoli and intervene with the absolutely pivotal exchange of gases resulting in inverse levels of oxygen and carbon dioxide in blood.

Fig. 4. Alveolus Gas Exchange

1.2.2 Respiration And Maintenance Of Chemical Balance

Respiration is one of the body’s stabilizing mechanisms whose role is to help in maintaining a firm internal environment that keeps all of the body cells functioning effectively. This is accomplished by supplying sufficient oxygen and removing extravagant carbon dioxide. Insignificant changes in the oxygen and/or carbon dioxide levels in the blood trigger processes that attempt to bring these levels back to normal.

Survival depends on the body’s capability to respond to constant changes in its environment. The body’s ability to reply to changes in its internal and external environments demands successive communication and interaction between the various organ systems of the body.
Changes in the body trigger complex responses. Various body systems often work together to return the internal environment to a normal state. Damage to lung tissues can limit the respiratory system’s ability to respond adequately to changes in oxygen and carbon dioxide levels in the body. This deteriorated capacity can lead to shortness of breath, fatigue, dizziness, and other symptoms. However, these symptoms have other possible causes, they are common problems for people living with lung cancer. To summarize, the lungs are vital organs; they are needful to sustain life.

The lungs take in required oxygen and cast off exorbitant carbon dioxide from the body. The respiratory and circulatory systems function together to preserve normal oxygen and carbon dioxide levels in all the tissues of the body. So, damage or removal of lung tissue may cause less effectiveness at the vital exchange of these gases that takes part in the lungs. The effects of this diminished function can be experienced throughout the body and cause a variety of symptoms.
Chapter 2: A Brief Overview Of Cancer

2.1 Cancer in General

Cancer is a state caused by the uncontrolled growth of cells. There are different kinds of cancer. These kinds are named according to the type of cell that is growing in an unchecked way. Cancer can arise from nearly any part of the body. There are more than 125 different types of cancer. Normal cells grow, disunite and die in a controlled way and with a prospective lifespan. In adults, most cells divide only to substitute old cells or to repair damage. Cancer cells have been harmed in such a way that they grow, divide rapidly and live more than healthy cells. In most cases, cancer leads to the formation of tumors, absonant clusters of cells. In addition, not all tumors are morbid for our body. These tumors that do not invade neighboring tissues or expand to other parts of the human body are called benign tumors. With some rare exceptions, benign tumors are not life threatening and do not cause disease. Malignant tumors are cancerous tumors. These tumors can invade and destroy neighboring tissues and organs, and spread to other parts of the body. This spread of cancer cells from one part of the body to another is called metastasis. In conclusion, malignant tumors have the ability to invade into neighboring tissues and expand to distant parts of the human body (metastasis) while benign tumors have not.

The National Cancer Institute estimates that approximately 8.9 million Americans alive today have been diagnosed with cancer at some time in their lives. According to the 2003 Cancer Facts & Figures report issued by the American Cancer Society, men in the United States have approximately a one in two chance of developing cancer in their lifetime. For women, the lifetime risk of developing cancer is just over one in three. In 2003, approximately 1,285,000 people in the United States were newly diagnosed with non-skin cancers. Cancer is the second
leading cause of death in the United States killing over half a million people each year. Approximately 16 million new cancer cases have been diagnosed since 1990. More specifically, cancer cells are unnatural because they comprise damaged genetic material. Inside each cell of our body exists our unique genetic blueprint. Every cell of a person’s body contains an identical copy of his or her unique Deoxyribonucleic Acid (DNA). There are some specific parts of DNA which are called genes. Each gene contains the message, the genetic code for a specific feature or function of the human body (Fig. 5).

Fig. 5. A typical human cell, the chromosomes and the DNA.
Everything from our body structure to body function is controlled by genes. They control physical features such as hair color, eye color, height and bone structure. Characteristics such as tolerance for pain, sensibility to certain diseases and natural athletic or musical capability are also controlled by genes. The functions of cells such as the ability to repair themselves, divide when new cells are needed and even to die in a specific time are all genetically controlled. During our lifetime, we are exposed to many things that can damage our DNA. Air pollution, chemicals in the environment, tobacco smoke, viruses and radiation from the sun or other sources can cause genetic damage (Fig. 6). The human body has especial mechanisms to fix genetic damage. Cancer supervenes when genetic damage either overwhelms or evades the body’s physical repair mechanisms. In a general aspect, it takes several different genetic flaws agglomerated over a long period of time for a cell to become cancerous. A cell’s life cycle is controlled by the genes. The abnormalities that lead to cancer are in the genes. These genes control when a cell divides and dies. In normal situations, a cell divides only when it gets a specific genetic message to do so. Thus, cells normally die according to a genetically programmed timeline. When genes that control cell division and death are damaged, cells divide uncontrollably and do not die in the normal timeline. This situation has the disastrous result that cancerous cells conglomerate in the body forming tumors. These tumors gradually crowd out normal cells. As a result, cancerous cells do not perform the necessary functions that healthy cells do. Therefore, as cancer cells crowd out healthy cells, body functions begin to fail.
2.2 The Metastatic Process

Cancer cells have many defining features that distinguish them from normal cells. One of the designated characteristics of cancer cells is their ability to invade neighboring tissues and to metastasize or spread to sites of the body distant from the tissue of origin. This process occurs when cancer cells abscond from the original tumor. The cells travel through the body with the help of circulatory or lymphatic system to another site of the body where they grow and multiply forming a new tumor. The several types of cancer are named according to the tissue from which they originate. When cancer cells metastasize and a new tumor appears in another tissue, it is still the same cancer (Fig. 7). To our point of interest, lung cancer often metastasizes and causes tumors in the liver, brain and bones. Thus, someone that suffers from lung cancer may have tumors in several different sites of his body. All of them are the result of the lung cancer, which has metastasized to other places.

Fig. 6. Normal and Cancer affected DNA.
In conclusion, all cancer cells share the same basic characteristics of uncontrolled growth and the ability to invade neighboring tissues and/or spread to distant sites. When a normal cell transforms into a cancerous cell that is the outcome of genetic damage. Radiation, environmental chemicals and other substances can all contribute to the genetic damage that leads to the development of cancer.
2.3 Generally For Lung Cancer

The more we learn about lung cancer the more we will be able to take efficient decisions about someone’s treatment and aftercare. Lung cancer explicates when normal lung cells maintain genetic damage that ultimately leads to uncontrolled cell multiplication. Lung cancer cells have the ability to invade neighboring tissues and spread or metastasize to distant parts of the body. If lung cancer is left unhealed, it eventually causes death. Sometimes lung cancer is named bronchiogenic cancer. The word bronchiogenic means that this cancer originates from the bronchi, the airways of the lungs. The majority of lung cancers begin in the cells that line the bronchi of the lungs. Lung cancer is differentiated in two types that are treated differently. Lung cancer is the number one killing type of cancer in the United States of men and women. This type of cancer kills more people in the United States every year than breast, colon, and prostate cancer combined. The American Cancer Society (ACS) appreciated there will be 172,570 new cases of lung cancer in the United States in 2005, and 163,510 lung cancer deaths. This means that every day of the year in this country, approximately 470 people are diagnosed with lung cancer and 450 people die of the deadly disease. Lung cancer is the main cause of cancer deaths not only in the United States, but all over the world. The World Health Organization (WHO) reports that over 1.1 million people die of lung cancer each year.

There are some risk factors for developing lung cancer. More specifically, this type of cancer develops when the cells that line the lungs suffer genetic damage. Several different chemicals and environmental factors that are capable of causing this kind of genetic damage have been identified. These substances can lead to lung cancer and are also named carcinogens. Lung cancer occurs frequently in people who are either current or former smokers. While the relationship between smoking and lung cancer is well-established, other factors also come into play. One out of every ten smokers develops lung cancer. Furthermore, one of every six people
who develops lung cancer never smoked. These statistics reveal that lung cancer development is a quite multi-factorial process. A majority of factors contribute to developing the disease. As mentioned before, one of them is smoking. Some are still the following, second-hand smokers, anyone who breathes in air that contains tobacco smoke, environmental carcinogens, substances in the environment capable of producing genetic damage that could contribute to the development of cancer, genetic factors, genes control how a person’s body handles carcinogens, how susceptible it is to genetic damage, and how capable it is of repairing damage that occurs, and finally age itself, genetic damage tends to accumulate over time.

2.4 Types Of Lung Cancer

Lung cancer derives from abnormal epithelial cells in the airways of the lungs. These cells form the covering over free surfaces in the body such as the airways. Lung cancer is divided into two main types based on how it looks under the microscope: Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC). SCLC and NSCLC have different patterns of growth and spread and are also treated differently.

2.4.1 Small Cell Lung Cancer

As the name hints, the cancerous epithelial cells of SCLC are incredibly small. Their appearance led to the term oat cell carcinoma to describe SCLC because the cells look like oat grains. SCLC is also sometimes called small cell undifferentiated carcinoma. Carcinoma is a term referring to any malevolent tumor that comes from epithelial cells. SCLC cells are sometimes spindle-shaped or polygonal. Some significant characteristics of SCLC are that there is a strong bonding between SCLC and tobacco smoking. Only about 1% of Small Cell Lung Cancer (SCLC) occurs in people who have never smoked. Furthermore, SCLC typically grows more quickly
than NSCLC does. Its common characteristic is that spreads to lymph nodes and metastasizes to other organs early in the disease process. SCLC tends to be originally responsive to chemotherapy and radiation therapy. Moreover, SCLC often occurs in one of the larger airways. Therefore, SCLC tumors are often located near the center of the lung. Finally, the majority of people with SCLC have metastases at the time of diagnosis.

### 2.4.2 Non-Small Cell Lung Cancer

The most common types of Non-Small Cell Lung Cancer (NSCLC) are: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. These major types of non-small cell lung cancer are grouped together because they have similar growth patterns and are healed in a similar way. Each of them has subtypes. Some fundamental characteristics of these types of NSCLC are being quoted below.

**Adenocarcinoma**

Adenocarcinoma cells have an appearance which is similar to that of a gland. The majority of these tumors produce a fluid called mucin. The incidence of adenocarcinoma has increased over the past three decades. It is not certain why this has occurred, but some influences may include changes in smoking habits, dietary patterns, environmental factors, and occupational factors. Its subtypes include acinar adenocarcinoma, papillary adenocarcinoma, bronchioloalveolar adenocarcinoma, and other mixed subtypes. Adenocarcinoma is the most common form of lung cancer in women and people who have never smoked. It is also the most common type in people less than age 50. Adenocarcinoma is the most common form of lung cancer associated with scathing of the lung tissue. Its tumors are most often in the outer district of the lungs. Finally,
adenocarcinoma accounts for approximately 40% of all lung cancers in the United States, and approximately 55% of NSCLC’s (Fig. 8).

Fig. 8. *Microscopic view of Adenocarcinoma type of NSCLC.*

**Squamous Cell Carcinoma**

This type of NSCLC is also referred as epidermoid carcinoma. Squamous Cell Carcinoma (SCC) has decreased in incidents over the past three decades, but is still the most common form of lung cancer among men who are current or former smokers. Its cells are large and flat. These tumors often produce a substance called keratin. SCC occurs most frequently in men and in people over age 65 of both sexes. It usually starts in one of the larger airways. Therefore, these tumors tend to be located in the central area of the lung. SCC tumors often invade neighboring structures and this type of NSCLC is strongly associated with tobacco smoking. It tends to
metastasize in other territories of the body, in other tissues, than other forms of NSCLC (Fig. 9). Finally, it is responsible for approximately 25-30% of lung cancer in the United States.

![Fig. 9. Microscopic view of Squamous Cell Carcinoma type of NSCLC.](image)

**Large Cell Carcinoma**

Large Cell Carcinoma’s (LCC) cells are the largest of the various types of NSCLC. Its cells are extremely immature and undifferentiated. There are several additional types of Large Cell Carcinoma including clear cell LCC, basaloid LCC, lymphoepithelioma-like carcinoma, and large cell neuroendocrine carcinoma. The prognosis for large cell carcinoma is less propitious than for other forms of NSCLC (Fig. 10). Large Cell Carcinoma (LCC) can come into view in any part of the lung. At last, this type of NSCLC is responsible for 10-15% of lung cancers in the United States.
Fig. 10. *Microscopic view of Large Cell Carcinoma type of NSCLC.*
Chapter 3: Lung Cancer Diagnosis And Staging

INTRODUCTION

The great reserve capacity of normal lungs permits cancerous lung tumors to grow for years without jeopardizing lung function. The lungs do not have many nerves to impart pain messages so a cancerous lung tumor can grow for many years without causing any symptoms. This means that the majority of people are not diagnosed with lung cancer until late in cancerous process. Furthermore, it is quite unfortunate that this long period of silent growth gives the cancer the opportunity to spread before it is diagnosed. It is very difficult for a lung cancer that has spread beyond the original size to cure. It is a common phenomenon people with lung cancer do develop symptoms. Most people diagnosed with lung cancer present symptoms related to the fatal disease but they occur late in the disease process. This silent growth of lung cancer has led scientists to develop various methods such as lung cancer screening in the past few years. The process that gives the opportunity to define whether the cancer has spread and to what extent is called staging.

3.1 Lung Cancer Screening And Early Detection

It is extremely important the topic of lung cancer screening. Cancer screening is the procedure that is performed on apparently healthy people to scan unrecognized cancer. The main purpose of this process is to identify people with the deadly disease so that the necessary steps are taken to possibly cure the disease or even improve the prognosis. There are some known lung cancer screening programs for colon cancer (sigmoidoscopy and occult blood tests), cervical cancer (Pap smears), prostate cancer (Prostate Specific Antigen (PSA) tests and physical
examinations) and for breast cancer (mammograms and monthly self-breast exams). It is notable that there is not cancer screening program for the number one cancer killer of both men and women – lung cancer. The reasons are complex and controversial. Yet, we should be worried about this fact if someone consider that lung cancer kills more people every year than breast, prostate, and colon cancer combined. The most commonly cited reason is based on the conclusions drawn from a lung cancer screening study performed in the 1970’s. Many learned scientists, researchers, and doctors have debated the validity of the trial design and its conclusions. Nevertheless, based on the controversial conclusions drawn from this trial, lung cancer screening programs are not supported or recommended by the responsible doctors. Despite the lack of support from public health agencies and national cancer organizations for lung cancer screening, many health experts try to persuade people, who may be at risk for lung cancer, to talk with their health care providers. People at greater risk of having a deadly disease, due to smoking history, occupation, or family history should inform their health care experts and advocates about their risk factors and discuss appropriate testing. It is widely accepted that most lung cancers are present for many years before symptoms of the disease appear. In the absence of early detection and lung cancer screening, most people who suffer from lung cancer cannot be cured because the disease is already too advanced at the time of diagnosis. Given this situation, it is at least theoretically acceptable that early detection and lung cancer screening would improve survival rates. Supporters of lung cancer screening and early detection suggest the following statements. The general public should be informed of lung cancer risk factors, and to be certain that those people in a very unfavorable situation understand their risk. An estimation of jeopardy such as an interview to collect information about lung cancer risk factors such as smoking history (tobacco smoking, crack, cocaine, marijuana), exposure to lung carcinogens, and family history of lung and other epithelial cancers. A possible testing program could have several components such as: imaging studies of the lungs and other early detection
tests; possible tests that could be used include standard chest x-rays, digital chest x-rays, helical/spiral Computed Tomography (CT) scans, tumor markers and sputum-based tests or other tests which are now being created. Tests to define sensibility to cancer; although we do not yet have such a test, this is an active area of research. Such testing might identify people in danger who may need close monitoring. Finally, smoking dismissal advisement and possible treatment to help those addicted to nicotine overcome their habit. There is a significant amount of work to be done to develop a widely accepted, cost-effective and valid lung cancer screening and early detection program. The majority of health providers and lung cancer experts strongly support that early detection is the answer to the question of how to improve lung cancer survival. The supporters of lung cancer screening programs have the hope of reaching a good point of development to diagnose people with lung cancer earlier in the disease process when there is a greater chance for treatment.

3.2 Lung Cancer Diagnosis

Diagnosing lung cancer is a mutable procedure. The tests performed and the order in which they are made depend on various factors including someone's medical history, findings on physical examination and presenting complaints. For some people, the diagnosis of lung cancer is straightforward. For other people, the procedure is more complicated. Each step in the diagnostic process and its result shows us what the next step will be. Approximately 5% of people who are diagnosed with lung cancer have no symptoms. They are usually diagnosed because of an unexpected finding during a physical examination, an abnormality on a routine chest X-ray, or some other incidental finding. However, the majority of people diagnosed with lung cancer seek medical attention because they are experiencing symptoms. To make things easier we could take that the diagnostic process is beginning at the point of experiencing symptoms. When a person pays a visit to the doctor, the investigation always begins into the
source of the problem with a medical history and a physical examination. Regarding someone's medical history, the doctor can give important information that shall help think through possible causes of the symptoms. Some significant points from a person's medical history may be the following: any problems a person had with his or her lungs in the past, personal smoking history and exposure to second-hand smoke, job history and/or exposure to potential lung carcinogens, a family history of lung cancer or other epithelial cell cancers, and when current symptoms started, and how they have changed over time. There is also another critical part of the diagnostic process and there is no other than physical examination. If someone has lung cancer, it is most likely to show the following symptoms: swollen lymph nodes, tenderness in the flank area (over the kidney), abnormal breath sounds in the lungs, tenderness and/or enlargement of the liver, fever, tenderness over any bones, swelling in the hands, feet, face, or ankles, skin changes such as rashes, dark areas, or a blue tint of the lips and nails, any findings that might indicate a primary tumor in a body organ other than the lungs and finally generalized or regional muscle weakness. There are many other possible physical findings a doctor will consider in deciding how best to proceed. Laboratory testing is usually included in the diagnostic process of someone who may have lung cancer. The specific tests doctor orders will depend on medical history, presenting symptoms, and physical findings.

3.2.1 Sputum Cytology

A sputum cytology test may be performed when lung cancer is suspected. A sample of sputum is collected first thing in the morning. Sputum is the thick, slippery fluid secreted by the airways; many people call sputum phlegm. The sample must come from deep in the lungs, so it must be produced by a deep cough. The sputum is placed on slides and stained in the laboratory. The slides are then examined under a microscope. The technologist examining the slides looks for cancer cells that may be contained in the sputum. Bacteria and other abnormal
cells may also be seen. The doctor may collect sputum samples on three consecutive days to increase the chances of finding cancer cells. When cancer cells are seen in a sputum cytology specimen, it is almost certain there is cancer in the lungs (Fig. 11). However, if cancer cells are not detected, this does not rule out the possibility of lung cancer because sputum cytology is positive in only 5-20% of people with lung cancer.

![Image](image_url)

**Fig. 11. Bronchial washing cytology of large cell carcinoma shows large pleomorphic obvious malignant cells with vesicular chromatin and prominent nucleoli.**

### 3.2.2 Tumor Markers

Tumor markers are substances in the blood that are found only when cancer is present, or are present in highly elevated amounts when cancer is present. CarcinoEmbryonic Antigen (CEA) is a tumor marker that is sometimes measured when lung cancer is suspected. However, CEA is erected in several types of cancer, not just lung cancer. Thus, an elevated CEA does not necessarily mean lung cancer is present. The definition of an erected CEA level is further complicated by the fact that smokers often have abnormally high CEA levels. Health care providers and scientists are working hard to find tumor markers for lung cancer that are both
sensitive to the presence of lung cancer and are specific for lung cancer. Sensitivity is the ability of a test to detect an abnormality if one is present. Specificity is a measure of how likely it is that a test irregularity intimates a specific disease. A sensitive and specific lung cancer tumor marker could eventually be used as diagnostic tool and as a screening test for people who are at risk but have no symptoms.

3.2.3 Imaging Tests

The imaging tests are performed to identify whether there is a cancerous tumor and therefore cancer. A significant amount of imaging tests can provide information which can help to define if a cancerous tumor is benign or malignant. The final finding of whether a tumor is a carcinoid one can only be taken by examining a tissue sample under the microscope. At last, they are useful to look for enlargement of regional lymph nodes, which could indicate cancerous spread.

CT Scans

CT scans (Computerized Tomographic scans) are x-ray imaging tests that may be used in the diagnostic work-up of suspected lung cancer. These imaging tests are able to scan smaller tumors than chest x-rays. They are also better able to determine the size, shape, and exact location of a tumor because they collect information in three dimensions instead of two. For those reasons, CT scans are better able to detect enlarged regional lymph nodes. When discovered and introduced for the first time in the diagnostic process the machines received autonomous x-rays of the human body, which were then put together by a computer to form three-dimensional images. The scanning process took 15-30 minutes, and the images were
affected by small movements during the study. In the early 1990’s, a new type of scanner was introduced, the spiral or helical CT scanner. This scanner is able to x-ray the entire chest in 20-30 seconds while the patient holds his or her breath (Fig. 12). The continuous nature of data collection by the computer and the reduced effects of movement make CT scans performed with helical/spiral machines clearer and better able to identify smaller tumors. In most circumstances, the high quality of helical/spiral CT scans make them more covetable than CT scans implemented with older scanning machines.

Fig. 12. Common appearances of lung metastases/lesions/nodules
Chest X-Rays

It has been proved that chest x-rays miss a significant number of lung tumors. Chest x-rays are often the first imaging process to be carried out when primary or metastatic lung cancer is suspected. This type of imaging procedure may miss a lung tumor if it is small or hidden behind a rib, collar bone, or the breastbone. They can also detect abnormalities other than tumors that may be related to lung cancer. For example, chest x-rays can detect a conglomeration of fluid around the lung, a state known as pleural effusion. Chest x-rays may also detect pneumonia, blocked airways or enlarged lymph nodes that are impeding air from reaching part of the lung. Even if the diagnosis of lung cancer is clear many health care providers and doctors want to take a chest x-ray to compare with previous and future chest x-rays. Future chest x-rays may help doctors monitor the course of your disease. During the last few years, a new type of chest x-ray called the digital chest x-ray has been innovated and been introduced in imaging process. The digital chest x-ray collects the image of the chest with a computerized detector instead of on a piece of film as is done with a conventional chest x-ray. The use of the detector instead of film allows for sharper, clearer images. Imaging specialists and researchers are also testing the use of computers to aid the reading of chest x-rays in an effort to pick up more lung tumors. This new innovated technology is called Computer-Assisted Diagnosis (CAD).The latest research results show that the combination of digital chest X-rays and CAD has the ability to greatly improve the efficiency and accuracy of chest x-rays in detecting lung tumors.
MRI Scans

MRI scans (Magnetic Resonance Imaging scans) use a large magnet (Fig. 13) instead of x-rays to produce three-dimensional images (Fig. 14). MRI is not commonly used on a daily basis and a work routine for suspected cancer. In special circumstances, this kind of imaging technique can be used to study a specific area of interest of the human body that is likely to be difficult to intervene a CT scan to produce an image. For example, areas of the body like the diaphragm or the uppermost part of the lung. However, CT is superior to MRI for imaging the structures in the chest.

Fig. 13. The MRI Scanner
PET Scans

PET (Positron Emission Tomography) scanning is a relatively new technology. The scan is taken by injecting sugar molecules that have a radioactive component into the human body. The amount of radiation used for these scans is very low (Fig.15). It is well known that cancer cells take up more sugar than normal cells because they are growing and disuniting rapidly. Therefore, areas of the body with cancer cells show up brighter on the scan than healthy tissues. Lymph nodes containing cancer cells, metastatic tumors and primary tumors all appear as bright spots on a PET scan. Apart from radiolabeled sugar, other substances are sometimes used for PET scans, but the theory behind the scans is the same. PET scans are sometimes used after chest x-rays or CT scans to differentiate between benign and cancerous tumors. They are not generally used as first-line diagnostic tests for lung cancer. This type of imaging technique is also useful for finding cancerous spread to regional lymph nodes and detecting distant metastatic tumors (Fig.16). However, there are circumstances other than cancer that cause
positive findings on PET scans. PET scan findings should be defined cautiously and compared to other test results.

Fig. 15. The PET Scan machine.

Fig. 16. Cancerous tumor in human lungs. The image is taken from a PET Scan machine.
3.2.4 Tissue Diagnosis

One of the surest ways to diagnose lung cancer and to get the right conclusions is to examine a sample of the tumor under the microscope. The procedure of acquiring a tissue sample is called a biopsy. To acquire a biopsy depends on the size and location of the tumor or lymph node being tested. There are some biopsy techniques below.

**Bronchoscopy**

Bronchoscopy is the most common biopsy technique for alleged lung cancer. This biopsy process involves putting a small, flexible tube called a bronchoscope into the larger airways of the lungs. This medical tool allows the doctor to look into the airways of the lungs and take a proper tissue sample (Fig. 17). Bronchoscopy is also quite useful for collecting tissue samples from tumors growing and growing in the larger airways of the human lungs or in the airways of the bronchial tree, usually in the central part of the lung. Samples of tissues from lymph nodes in and around the lungs can be collected with a bronchoscope. In conclusion, this type of medical invasive procedure is generally performed as an outpatient process. Autofluorescence bronchoscopy is a modified bronchoscopy procedure that uses fluorescent light to detect contingently cancerous areas of the airways. Thus, tumors and other abnormal cells shine when they are exposed to specific types of fluorescent light. Autofluorescence bronchoscopy enables health care providers, doctors and health specialists etc. identify suspicious areas in the airways to sample. This technique is particularly useful for patients whose sputum cytology test showed cancer cells, but imaging studies failed to show a lung tumor. Finally, this kind of bronchoscopy is also better than standard bronchoscopy for detecting lesions which may develop into lung cancer.
Transthoracic Needle Biopsy

These types of biopsies are usually appropriate for people who have tumors near the surface of the lung that would be difficult to reach by bronchoscopy. Transthoracic needle biopsy is sometimes known as Fine Needle Aspiration (FNA) biopsy. In this process, a needle enters the chest wall into the lung tumor. With the needle doctors collect small tissue samples (Fig. 18). This procedure is performed using either computerized tomography (CT) or fluoroscopy (another x-ray technique) to help the doctor direct the needle into the precise location of the tumor. Local anesthesia is used to numb the skin where the needle is inserted, and a mild sedative is used to relax the patient. The process is usually executed on an outpatient basis.

Fig.17. Typical bronchoscopy image.
Mediastinoscopy

It is a surgical procedure in which a rigid instrument called an endoscope is inserted through a small scission at the base of the neck or near the breastbone into the central area of the chest called the mediastinum. The mediastinum is the area in the interior of the chest which contains the heart, the large blood vessels entering and leaving the heart, the trachea, the esophagus, and several lymph nodes that drain lymph fluid from the lungs (Fig. 19). This process is often used for both diagnosis and staging because sampling the lymph nodes of the mediastinum is an important part of defining lung cancer stage. Mediastinoscopy is usually being carried out as a diagnostic test in people who have centrally located lung tumors that can be reached from the mediastinum. A significant amount of biopsies of the primary tumor and mediastinal lymph nodes are taken during the procedure. This kind of surgical procedure is performed with general anesthesia and requires hospitalization overnight.
Thoracotomy

In very rare cases doctors are unable to biopsy to a potentially malignant tumor in the lung by carrying out one of the above-mentioned methods. In these instances, a thoracotomy may be performed. A thoracotomy is a major surgical procedure and requires total anesthesia for the patient. The chest opens and the cell of the ribs is dimmed to show the lungs. A biopsy is performed on the tumor and the malignant tumor is observed under the microscope whereas the patient is still in the surgical room (Fig. 20). If cancer is found, the doctor will take a sample from regional lymph nodes to determine if a surgical cure is possible. If surgical cure is possible, a potentially therapeutic operation will be performed. Diagnosis and treatment are being carried out at the same time in this unusual situation. Staying in the hospital after a thoracotomy is one week or more.
Thoracoscopy

It is another surgical procedure in which an endoscope is inserted into the chest space. Thoracoscopy has a very limited utility in the diagnosis of lung cancer, but it is sometimes used for biopsy in some possibly malignant tumor or near lymph node. This type of diagnostic method has the advantages of allowing the surface of the lung to be examined and permitting sampling of any pleural effusion that may be present (Fig. 21). Video-Assisted Thoracoscopy (VATS) is a technique in which a tiny video camera is inserted into the chest by a small incision separate from the incision used for the thoracoscope. Images from the chest cavity are projected onto a screen during the procedure to give the doctor a better view of the area (Fig. 22). These procedures are performed with the patient being totally unconscious and require an overnight stay in the hospital after the end of the surgery.
Fig. 21. Typical image of thoracoscopy procedure.

Fig. 22. Typical image of vide-assisted thoracoscopy (VATS) procedure.
3.2.5 The Lung Cancer Staging Process

It is the process of classifying the extent of spread of the cancer from the original tumor to other regions of the human body according to standard criteria. This type of process is very important for two reasons: helps doctors to find out which treatment is best suited to the patient and also what the progress of the patient's illness (prognosis) is likely to be. The lung cancer staging is the primary factor influencing the prognosis of the disease. Lung cancer stages range from I through IV. In general, the lower the stage, the less the cancer has spread. The higher the stage, the more extensive is the spread of the disease. The main trend in prognosis is the lower the stage, the better the prognosis. There are three factors that are used to determine lung cancer stage. These factors are expressed using the TNM classification system. The three factors of the TNM system are:

T: tumor characteristics including size, location, and local invasion

N: regional lymph node involvement

M: metastasis status

This type of procedure, lung cancer staging, generally doctors try to establish factor M as early as possible in this process. This is why some distant metastasis goes to the patient directly to stage IV. The presence of distant metastasis is usually established with imaging tests, which are much less invasive than procedures such as bronchoscopy and mediastinoscopy that are used to establish lymph node involvement and tumor characteristics. If distant metastasis is present and the stage of a patient is IV then it does not need to continue further the staging procedures. Therefore, determining a person's M-status is taken up early in the staging process to spare people who are stage IV unnecessary procedures.
3.2.6 The Metastatic Status

The state of metastasis (M) is defined as:

M0: No distant metastasis found.

M1: Distant metastasis is present.

Some physical findings and presenting symptoms may raise suspicion of metastatic disease in a specific organ or area of the body. So scans will be performed in the specific area of interest or organ. However, metastatic disease does not show symptoms at this stage of diagnosis, which situation requires extensive research for distant metastatic tumors. The imaging tests used are listed below:

Positron Emission Tomography (PET) scans - whole body, Computed Tomography (CT) scans - abdomen, pelvis, and brain, Magnetic Resonance Imaging (MRI) scans - brain, bone scans - whole body and ultrasonography - abdomen and liver. CT, MRI, and PET scans were discussed in the previous section under Imaging Tests. Ultrasonography uses special frequency sound waves to visualize internal organs. Bone scans are similar to PET scans. A radioactively labeled substance that is taken up by actively growing and dividing cells is injected into the body. A scan is later taken of the entire body to look for ‘hot spots’ in the skeleton. Hot spots are areas of the skeleton that have taken a large dose of the radiolabeled chemical, which may be due to a metastatic disease.
3.2.7 Determining Regional Lymph Node Involvement

As far as the lymph nodes are concerned, two additional terms are important to understand the staging of regional lymph node involvement. Ipsilateral refers to lymph nodes on the same side of the chest as the primary tumor. Contralateral refers to lymph nodes on the opposite side of the chest as the primary tumor. Regional lymph node status is divided into the following categories.

N0: No evidence of cancer in the regional lymph nodes

N1: Cancer in the ipsilateral hilar lymph nodes

N2: Cancer in the ipsilateral mediastinal lymph nodes

N3: Cancer in the contralateral lymph nodes or in the supraclavicular area

Regional lymph nodes can be sampled and staged with the following procedures:

Mediastinoscopy, thoracoscopy and VATS, bronchoscopy and thoracotomy.

As imaging technologies are evolving more and more, experts continue to study the correlation between regional lymph node staging as determined by imaging studies compared to tissue sampling. Although tissue sampling remains the standard for staging, especially in patients who are candidates for surgery, imaging techniques will probably have a more decisive role in lung cancer staging in the future. Such a combined imaging technology, which is extremely promising for the future, is CT and PET scanning known as in-line CT-PET scanning. Our first results show that the combined imaging power of these two techniques is greater and more efficient in the lung cancer staging process than running each one separately.
3.2.8 Determining Tumor Characteristics

The categories for lung cancer tumor classification take into account the size, location, and local invasiveness of the primary tumor. Tumor characteristics are decided using the same methods used for diagnosis and evaluation of the regional lymph nodes. The specific tests used vary from one person to another depending on his or her unique history, symptoms, and physical findings. The tumor categories are:

T0: No evidence of primary tumor

Tis: Carcinoma in situ

T1: Tumor that is less than 3 cm (1½ inches) in size and is completely surrounded by lung tissue

T2: Tumor that is larger than 3 cm (1½ inches) but is still surrounded by lung tissue and is not invading the chest wall or any of the structures in the mediastinum

T3: Tumor of any size that invades the chest wall, diaphragm, or the pleura of the mediastinum or heart; a T3 cancer is potentially respectable (surgically removable)

T4: A tumor of any size that invades the structures of the mediastinum or a vertebral body (a backbone)

The area where the trachea is divided into right and left main bronchus is called carina. If the tumor is close to the carina, it may not be operable if the remaining airways cannot be needled together. Therefore, tumors involving the carina are T4 tumors. Tumors associated with a malignant pleural (around the lung) or a pericardial (around the heart) effusion are also T4 tumors, as are separate tumor nodules in the same lung lobe. T4 tumors are generally inoperable.
Chapter 4: Lung Cancer Treatment

INTRODUCTION

Lung cancer is currently cured by three forms of treatment. These are: surgery, chemotherapy and radiotherapy. They are used on the patient in combination or separately depending on the type of lung cancer from which he or she suffers and the stage of illness. In this chapter basic concepts will be discussed about each of these forms of therapy and their uses in the treatment of lung cancer.

4.1 Surgery For Lung Cancer

Surgery is a local treatment for lung cancer. It is used for possible treatment or to alleviate symptoms. Lung cancer that has not spread can be cured by surgery, which is often combined with chemotherapy and radiation therapy. A summary of surgical procedures used to treat lung cancer is presented in this chapter. Studies have shown that greater experience with lung cancer treatment is associated with more successful surgical outcomes. Candidate patients for surgery should find a surgeon with experience in thoracic surgery and it is preferable that the surgery be done in a hospital where there is a care for the operated patients.

4.1.1 Surgical Chest Procedures

The most common surgery performed for lung cancer is lobectomy. It is the removal (resection) of the lobe of the lung affected by cancer. Pneumonectomy is the surgical removal of the entire lung affected by cancer. This surgery is only done when the cancer cannot be completely removed by lobectomy. These two procedures are generally preferred by less extensive surgical
procedures, if the patient can, of course, tolerate them. Prolonging lung problems such as Chronic Obstructive Pulmonary Disease (COPD) or chronic bronchitis may prevent the use of these extensive lung surgeries. The process of removing a wedge-shaped section of tissue that surrounds the cancerous tumor is called wedge resection. It is performed on growths near the surface of the lung when a more extensive procedure cannot be tolerated. A segmentectomy or bronchopulmonary segment resection is another lung sparing operation which comprises removing the part or part of the lung lobe containing the cancerous tumor. The procedure used to remove tumors in the main airways (the right and left main bronchus) is called sleeve resection (Fig. 23).

Fig. 23. *The figure above demonstrates the different types of procedures (resections) that can be used to remove lung cancers.*

The area with the tumor is removed and the ends on either side are sewn together to re-establish airflow. All lung cancer operations include examination and removal of lymph nodes in the mediastinum. Removal of multiple lymph nodes in the area is called mediastinal lymph node
sampling. Removal of nearly all the lymph nodes is called a mediastinal lymph node dissection. None of these procedures assures the removal of all cancer cells that may be present. Thoracotomy is an open chest procedure that is used to perform surgical resection of lung cancer. The chest cavity is opened, the ribs are separated, and the lungs are exposed. A thoracotomy is major surgery and usually requires a hospital stay of at least one week. Video-assisted thoracoscopy (VATS) is a less invasive procedure that can be used for some lung cancer resections. The procedure is performed through a rigid tube called a thoracoscope, which is inserted into the chest through one or more small incisions. A tiny video camera is also inserted into the chest through another small incision. Pictures of the chest cavity are projected onto a screen in the operating room to give the surgeon a better view of the area. VATS is performed under general anesthesia, but the chest cavity is not opened and the ribs are not separated. Early studies indicate VATS may cause less postoperative pain than thoracotomy.

4.1.2 Surgical Side Effects and Possible Complications

All surgical procedures cause postoperative pain. The severity of the pain depends on the extent of the procedure, the surgical technique used to perform the operation, and your personal sensitivity to pain. Immediately after surgery, strong pain medicines are often needed. Morphine (MSIR, MS-Contin®, Roxanol®, Oramorph-SR®), oxycodone (Oxycontin®, Roxicodone®), hydromorphone (Dilaudid®, Hydrostat®), and fentanyl (Duragesic®, Fentanyl Oralet®, Sublimaze®, Innovar®) are examples of medicines that may be used. As the pain becomes less intense, less painful painkillers are used like codeine, hydrocodone (Vicodin®, Lortab®), dihydrocodeine (DHC), oxycodone (Percodan®, Percocet®, Tylox®, Roxiprin®), meperidine (Demerol®), and propoxyphene (Darvon®, Darvocet®). Eventually, you will be
switched to a mild pain reliever such as acetaminophen (Tylenol®), ibuprofen (Advil®, Motrin®, Nuprin®), or naproxen (Naprosyn®) until your pain is gone. Possible complications of chest surgery are: air leakage from the lung, fluid accumulation in the lung (pulmonary edema), bleeding, poor inflation of an area of the lung (atelectasis) and infection. Appropriate therapy is needed if some of these complications arise.

4.2 Chemotherapy For Lung Cancer

Chemotherapy is broadly defined as the use of medicines to treat disease. In the field of cancer, chemotherapy is the use of drugs (medicines) to kill cancer cells. Cancer chemotherapy drugs are also called cytotoxic drugs. Cancer cells divide very quickly, at a higher rate than most normal cells of the body. Drugs for chemotherapy use this very feature of cancer cells to cause their death by leaving healthy cells intact. Some cytotoxic drugs interfere with the cell division cycle. This prevents cancer from being reproduced again. Other chemotherapy drugs cause genetic damage the cancer cell is unable to repair ultimately leading to cell death. Although chemotherapy drugs work in different ways, they all target mechanisms active in cells that are rapidly growing and dividing. Chemotherapy drugs with different mechanisms of action are frequently used together to increase the overall response to treatment. Cancer chemotherapy is systemic therapy, meaning the entire body is exposed to the treatment. Chemotherapy is used when there is clear evidence that the cancer has grown beyond the normal tumor or if there is reason to suspect that there may be unidentified cancer cells (micro-metastasis) in the body. Chemotherapy may be used in lung cancer treatment for the following reasons: to prevent cancer spread, to slow cancer growth and prolong life, to shrink tumors and relieve disease related symptoms and to achieve a complete response and potential cure. Many chemotherapy
drugs must be given directly into the blood stream by an intravenous line (Fig. 24). This route of administration (how a drug is given) is necessary for chemotherapy drugs that would be broken down and inactivated by the digestive processes of the stomach and intestines. However, some chemotherapy drugs can be taken by mouth without any loss of anti-cancer activity. Chemotherapy drugs are administered on different schedules. Some drugs are given over a few hours; others are given in continuous drip over a few days. Whatever the specific administration schedule, most chemotherapy drugs are given in cycles. Drugs given in cycles are administered periodically with breaks between doses. Each complete administration of the chemotherapy drugs someone takes (including breaks) is called a treatment cycle. Chemotherapy drugs are given in cycles because it takes time for the drugs to have the desired effect on the cancer cells. Cyclic treatment also allows normal cells time to recover between chemotherapy treatments. Chemotherapy treatments may be weekly, biweekly, monthly, or on another schedule. The time between treatment cycles depends on the drugs used. The number of cycles used in a treatment protocol also depends on the drugs used.

**Peripheral Venous Catheter**

![Peripheral Venous Catheter](image)

Fig. 24. *Enlarged peripheral venous catheter.*
4.3 Side Effects of Chemotherapy

Chemotherapy can cause several serious side effects. Many of the side effects are related to the fact that these drugs do not selectively kill cancer cells but interfere with the processes of any rapidly dividing cell. That is why the body tissues that normally grow and divide can quickly be destroyed. For example, bone marrow cells that produce red blood cells, white blood cells and platelets can be damaged by chemo treatment. The cells lining the inside of the mouth and throat also divide rapidly and are susceptible to chemotherapy drugs. As a result, many people on chemotherapy experience mouth sores, dryness, and taste changes. Hair follicles can also be damaged by chemotherapy drugs leading to partial or complete hair loss. Each chemotherapy drug has the potential to cause different side effects. The list of possible side effects associated with a particular chemotherapy drug is called its side effect profile. The number and severity of side effects experienced from any given drug varies greatly from person to person. The drug, its dosage, and your body’s reaction to the drug influence the occurrence of chemotherapy side effects and their severity. Possible side effects associated with various chemotherapeutic drugs used to treat lung cancer are listed below: hair loss, fatigue, loss of appetite (anorexia), constipation, mouth sores, dry mouth, taste changes, nausea and vomiting, numbness, tingling, pain in the hands and feet (peripheral neuropathy), mental fatigue, slow thinking, faulty memory, diarrhea and myelosuppression including anemia (low red blood cell count), neutropenia (low white blood cell count), and thrombocytopenia (low platelet count).

4.4 Radiation Therapy For Lung Cancer

In this dissertation we focus on the subject of radiation therapy for lung cancer. Let’s go further into this subject. Many people with lung cancer are treated with radiation therapy. Radiotherapy
uses high-energy radiation called ionizing radiation to stop cancer cell division. This prevents the further formation of cancer cells. Ionizing radiation reacts with the water inside the cells causing damage to the genetic material. Healthy cells can repair this damage while cancer cells do not. The damaged cancer cells eventually die as a result. The dose or amount of energy deposited in a treatment area is expressed in rads or gray (Gy).

\[1 \text{ Gy} = 100 \text{ rad}, \ 1 \text{ rad} = 0.01 \text{ Gy}\]

The dose of radiation given for cancer therapy is several thousand times greater than the amount of radiation you are exposed to during an imaging x-ray. A machine called a linear accelerator is usually used to deliver radiotherapy. Radiation therapy is a focused form of cancer treatment in the area of interest. This means it affects only cells in the treatment area as opposed to a systemic therapy (like chemotherapy) that affects cells throughout the body. Radiation therapy is frequently used in lung cancer in combination with surgery and/or chemotherapy. The goal of radiotherapy used in this way is to cure the cancer. Radiotherapy can be used to: increase the response of cancer cells to treatment by administering it along with or following chemotherapy, destroy any remaining cancer cells that may be left behind after cancer surgery and shrink a tumor before surgery. Radiotherapy is also used as a therapy to alleviate the pain, to relieve disease-related symptoms and prolong life when cure is not possible. Alleviated radiation therapy is often lower dose and given over a shorter period of time than adjuvant radiotherapy. Radiation therapy is also used to treat or prevent brain metastasis. Radiation treatments can be given externally or internally. External beam radiation is radiotherapy delivered from outside the body. Currently, standard radiation treatments for lung cancer are delivered externally. Radiation oncologists are doctors who specialize in the use of radiotherapy to treat cancer. Planning is an important aspect of radiotherapy. A radiation oncologist decides the total dose of radiation you will receive and the treatment schedule. The total radiation dose is divided into smaller doses or fractions that are administered over a period of weeks. Fractionating the total
radiation dose limits damage to healthy tissues without compromising treatment effectiveness. The total radiation dose and treatment schedule depend on: other treatments you are receiving, the size and location of the tumor(s), your overall health and the presence of distant metastasis. The time off gives normal cells time to recover from radiation damage. Treatments continue for 2-7 weeks depending on the intent of the therapy. It is very important not to miss any scheduled treatments. Missed treatments decrease the total radiation dose delivered and can reduce overall treatment effectiveness. Before the external radiation treatments begin, the patient will go through a process called simulation. Simulation allows doctors to precisely map the radiotherapy target area and limit the exposure of healthy tissue to the radiation.

4.5 Side Effects of Radiation Therapy

The side effects in general of radiation therapy for lung cancer concern the destruction of healthy tissues in the body. Small fractional doses lead to fewer and less painful side effects. Most side effects from radiotherapy are local, that is, they occur only in the treatment field. Some of them are mentioned below: fatigue – usually begins the second or third week of treatment and often increases over time during treatment, cough, chest discomfort, shortness of breath, loss of appetite, hair loss in the treatment field, skin problems in the treatment field – redness, irritation, dryness, itching, skin darkening, mouth problems – mouth sores, dry mouth, cavities in the teeth, impaired mental functions (with whole brain radiation) and sore throat, hoarseness and/or difficulty swallowing (esophagitis).The skin is a rapidly dividing tissue, which makes it susceptible to radiotherapy. Skin in the treatment field often gradually becomes red or darkened, much like a sunburn or tan. The area may be sore, dry. Radiation to the lungs is associated with short-term side effects and late complications that can develop after treatment
is completed. Esophagitis is inflammation of the esophagus (the tube that takes food from the mouth to the stomach). Radiotherapy directed toward the center of the chest can damage the cells lining the esophagus. This causes sore throat, pain, and difficulty swallowing. Pain medication may be needed. The lining of the esophagus usually heals within one month after treatment has been completed. Radiation pneumonitis occurs in 2-9% of people who receive radiation therapy for lung cancer. It is the result of damage to the lining of the airways and air sacs. Women are slightly more prone to develop this complication than men are. Smoking increases the risk for both men and women. Radiation pneumonitis can occur anytime in the six months after completion of therapy but most commonly occurs 4-6 weeks after treatment completion. The symptoms of radiation pneumonitis are cough, low fever, shortness of breath, and/or pain with breathing. Radiation fibrosis may develop after radiation pneumonitis as the body tries to repair previously healthy lung tissue. Radiation fibrosis is lung tissue scarring that is the result of ongoing inflammation. Fibrosis develops gradually, usually over a period of 1-2 years after radiotherapy. Physical therapy and pulmonary rehabilitation can help prevent or alleviate the symptoms of radiation fibrosis.
Chapter 5: The LINAC Machine

INTRODUCTION

Since the discovery of X-rays by Roentgen in 1895, the technology of radiation production has been aimed towards high energy and intensity photons and more lately toward intensity modulated beam delivery and computerization. The first 50 years of radiotherapy has been characterized by slow technological progress and mainly based on X-ray tubes, Van de Graff generators and betatrons. As the technology of radiotherapy evolved, linear particle accelerators emerged. A Linear Particle Accelerator (often shortened to LINAC) is a type of particle accelerator that greatly increases the kinetic energy of charged subatomic particles or ions by subjecting the charged particles to a series of oscillating electric potentials along a linear beamline. The principles for such machines were proposed by Gustav Ising in 1924, while the first machine that worked was constructed by Rolf Widerøe in 1928 at the RWTH Aachen University. The development of linear accelerators was carried out by mostly two groups: W.W. Hansen’s group at Stanford University in the U.S.A and D.D. Fry’s group at Telecommunications Research Establishment in the U.K. Linacs have many applications: they generate X-rays and high energy electrons for medicinal purposes in radiation therapy, serve as particle injectors for higher-energy accelerators, and are used directly to achieve the highest kinetic energy for light particles (electrons and positrons) for particle physics.

5.1 General Description Of A Medical Linear Accelerator

Linac-based radiation therapy for cancer therapy began with treatment of the first patient in 1953 in London at Hammersmith Hospital, with an 8 MeV machine built by Metropolitan-
Vickers, as the first dedicated medical linac. A short while later in 1955, 6 MeV linac therapy from a different machine was being used in the United States. The linear accelerator, in strict terminology is the part of the radiation treatment machine in which electrons are accelerated up to the required energy, which may be from 4 MeV for a low-energy machine to a few tens of MeV for a higher-energy machine. In general, the term linear accelerator is used as a description of the whole system used for the delivery of the radiotherapy. The main parts of a linear accelerator used for medical purpose are the following: the unit which carries the linear accelerator waveguide, the beam defining system and also the patient support system. There is also the control unit which is located outside the treatment room and finally the high-voltage supply and pulse modulator which is mounted on the accelerator stand. These are the main parts and systems of the accelerator that are needed for the generation of the radiation beam. Several essential but collateral systems are the following: including control systems, interlock and cooling systems, and the vacuum system. Electrons are produced by a thermionic emission in the electron gun, which injects a pulse of electrons into the electron accelerator. This is a waveguide structure in which energy is transferred to the electrons from the RF fields set up by microwaves, typically at a frequency of 3000 MHz (100 mm wavelength in free space). The microwave radiation is supplied in short pulses, and this is generated by applying high-voltage pulses of about 50 kilovolts from the pulse modulator to the microwave generator, which is more frequently a magnetron valve. In some higher-energy accelerators a klystron valve is used as the microwave power source. The electron gun and the microwave source are pulsed so as that the high-velocity electrons are injected into the accelerated waveguide at the same time as it is energized by the microwaves. Some linacs have short, vertically mounted waveguides, while higher energy machines tend to have a horizontal, longer waveguide and a bending magnet to turn the beam vertically towards the patient. Medical linacs use monoenergetic electron beams between 4 and 25 MeV, giving an X-ray output with a spectrum of energies up
to and including the electron energy when the electrons are directed at a high-density (such as tungsten) target. The energy of the resultant x-rays is approximately the energy of the electron when they hit the target. The final speed of these electrons is determined by the electrical potential drop across the linear accelerator. The electric potential is on the order of 6,000,000 volt, or “6 Megavolt”, or “6 MV”. Compare this to the standard electric potential which powers a toaster or refrigerator of 120 volt. Therefore, the energy of the x-rays emitted from the LINAC is approximately 6,000,000 volt. Higher x-ray energies mean larger electrical potentials which leads to a longer accelerating cavity. The length of a typical 6 MV LINAC is approximately 1,83 meters. It is these high energy x-rays which are used to irradiate the patient’s tumor. So, a linear accelerator (LINAC) customizes high energy x-rays or electrons to conform to a tumor’s shape and destroy cancer cells while sparing surrounding normal tissue. It is used to treat all parts/organs of the body. The electrons or X-rays can be used to treat both benign and malignant disease. The LINAC produces a reliable, flexible and accurate radiation beam. However, this wasn’t originally the case. The cobalt-60 therapy machine was the first practical megavoltage therapy machine used in radio therapy that was developed in Canada in the 1950’s. It has been a massive innovation in research for higher photon energies. The cobalt-60 unit was consolidated to the top of radiotherapy machines for a significant amount of years. It is characterized with features extremely useful for radiotherapy. These are: relatively high specific activity, long half-life, simple means of production and high energy gamma ray emission. In contrast to cobalt-60 machines, linacs have added characteristics, such as high dose rate modes, dynamic motion of the collimators while the beam is ON, electron arc therapy, multileaf collimator leaves, gantry and couch. They have multimodality capabilities and increased use of computer logic and microprocessors in the control systems of those machines. However, despite all the advantages linacs have, compared to cobalt-60, the latter used to have an important place in the radiotherapy “arsenal”, for several years. Above all, due to lower
capital, installation and maintenance costs of cobalt-60 machines compared to linacs. Thus, the versatility of LINAC is a powerful advantage over cobalt therapy as a treatment tool. In addition, the device can simply be powered off when not in use. There is no source requiring heavy shielding – although the treatment room itself requires considerable shielding of the walls, doors, ceiling etc. to prevent escape of scattered radiation. Prolonged use of high powered (>18 MeV) machines can induce a significant amount of radiation within the metal parts of the head of the machine after power to the machine has been removed (i.e. they become an active source and the necessary precautions must be observed). It features several built-in safety measures to ensure that it will not deliver a higher dose than prescribed and is routinely checked by a medical physicist to ensure it is working properly. Apparently, the linear accelerator (LINAC) is the device most commonly used for external beam radiation treatments for patients with cancer. The high energy x-rays are shaped as they exit the machine to conform to the shape of the patient’s tumor and the customized beam is directed to the patient’s tumor. The beam is usually shaped by a multileaf collimator that is incorporated into the head of the machine. The patient lies on a moveable treatment couch and lasers are used to make sure the patient is in the proper position. The treatment couch can move in many directions including up, down, right, left, in and out. The beam comes out of a part of the accelerator called a gantry, which can be rotated around the patient. Radiation can be delivered to the tumor from any angle by rotating the gantry and moving the treatment couch. The acceleration cavity is mounted on a gantry as assumed which allows the LINAC to be pointed at a single point in space, however with the freedom to rotate through a full circle (Fig. 25). The LINAC can be used to treat lesions anywhere in or on the patient’s body. The LINAC is used to treat all body sites, using conventional techniques, Intensity-Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), Image Guided Radiation Therapy (IGRT), Stereotactic Radiosurgery (SRS) and Stereotactic Body Radio Therapy (SBRT) (Fig. 26).
LINAC (schematic diagram)

Fig. 25. Typical schematic diagram image of a medical LINAC machine.

Medical Linear Accelerator (LINAC)

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Fig. 26. Image of a medical LINAC machine.
5.2 What Is Important When Using Linear Accelerator Equipment

**Strength of the technology: MeV.** The greater the strength of the machine, the further into tissue it can penetrate. The strength of the machine may be a function of the method it uses to deliver the radiation and not necessarily equal to the MeV rating.

**Imaging technology utilized.** MRI technology is considered the gold standard when imaging to target a brain tumor. MRIs provide an unparalleled view inside the body. MRI scans are able to see normal tissue versus brain tumor tissue. CT scanning uses X-ray technology to scan a tumor. Tumor borders cannot be seen on a CT scan. Bone nearby a tumor will obscure clear CT imaging of the tumor. The precise details of soft tissue are less visible on CT scans than on MRI scans. Some linear accelerator technology can only use CT scans. There are experts that believe this may contribute to permanent side effects and inferior results for tumor growth control with linear accelerator technology, that are not as good as with Gamma Knife® technology. Other linac technology can fuse MRI and CT images.

The first patient treated for retinoblastoma with linear accelerator radiation therapy was Gordon Isaacs in 1957, in the U.S. (Fig. 27). Other patients had been treated by LINAC for other diseases since 1953. Gordon's right eye was removed on January 11, 1957 because cancer had spread there. His left eye, however, had only a localized tumor that prompted Henry Kaplan to treat it with the electron beam.
Fig. 27. Historical image showing Gordon Isaacs, treated for retinoblastoma with linear accelerator radiation therapy (in this case an electron beam), in 1957, in the U.S.
Chapter 6: How Radiation Therapy Is Carried Out In Lung Cancer?

INTRODUCTION

The practice of radiotherapy requires not only excellent clinical skills but also appropriate technical expertise. In this part, the following issues will be mentioned: some factors contributing to making good clinical judgements, the specialist knowledge required to plan radiotherapy treatment.

6.1 Target Volume Definition

A common international language for describing target volumes is found in International Commission on Radiation Units (ICRU). These contain clear definitions to enable centers to use the same criteria for delineating tumors for radiation so that their treatment results can be compared.

6.1.1 Gross Tumor Volume

Gross Tumor Volume (GTV) is the primary tumor or other tumor mass shown by clinical examination, at examination under anesthetic or by imaging. GTV is classified by staging systems. Tumor size, site and shape may appear to vary depending on the imaging technique used and an optimal imaging method for each particular tumor site must therefore also be specified. A GTV may consist of primary tumor (GTV-T) and/or metastatic lymphadenopathy
(GTV-N) or distant metastases (GTV-M). GTV always contains the highest tumor cell density and is absent after complete surgical resection.

### 6.1.2 Clinical Target Volume

Clinical Target Volume (CTV) contains the GTV when present and/or subclinical microscopic disease that has to be eradicated to cure the tumor. CTV definition is based on histological examination of post mortem or surgical specimens assessing extent of tumor cell spread around the gross GTV. The GTV-CTV margin is also derived from biological characteristics of the tumor, local recurrence patterns and experience of the radiation oncologist. A CTV containing a primary tumor may lie in continuity with a nodal GTV/CTV to create a CTV-TN (e.g. tonsillar tumor and ipsilateral cervical nodes). When a potentially involved adjacent lymph node which may require elective irradiation lies at a distance from the primary tumor, separate CTV-T and CTV-N are used e.g. an anal tumor and the inguinal nodes. CTV can be implied by the dose level prescribed, as for example, CTV-T50 for a particular CTV given 50 Gy. For example, for treatment of breast cancer, three CTVs may be used for an individual patient: CTV-T50 (50 Gy is prescribed to the whole breast) CTV-T66 (66 Gy to the tumor bed) and CTV-N50 (50 Gy to regional lymph nodes). Variation in CTV designation is the greatest geometrical uncertainty in the whole treatment procedure. Studies comparing outlining by radiologists and oncologists have shown a significant inter-observer alterability for both the GTV and/or CTV at a variety of tumor sites. This is greater than any intra-observer variation. Published results for nasopharynx, brain, lung, prostate, medulloblastoma and breast all show important variations in the volumes outlined by different clinicians. Improvements can be made with training in radiological anatomy which enables clinicians to discern blood vessels from lymph nodes and
to identify structures accurately on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). Joint outlining by radiologists and oncologists can improve consistency and ensure accurate rendition of imaging of the GTV.

6.1.3 Planning Target Volume

If the patient moves or internal organs change in size and shape during a fraction of treatment or between fractions the position of the CTV may also move. Thus, to ensure a homogeneous dose to the CTV throughout a divide into components course of irradiation, margins must be added around the CTV. These permit for physiological organ motion (internal margin) and variations in patient positioning and alignment of treatment beams (set-up margin), creating a geometric planning target volume. The Planning Target Volume (PTV) is used in treatment planning to select suitable beams to ensure that the prescribed dose is actually delivered to the CTV.

6.1.4 Organ Motion/Internal Margin

The changes in organ motion may be small (e.g. brain), larger and prospective (e.g. respiration or cardiac pulsation), or unpredictable (e.g. rectal and bladder filling). In case of treating lung tumors, the displacement of the CTV caused by respiration can be addressed in a variety of ways: by increasing the CTV-PTV margin eccentrically to include all CTV positions during a respiratory cycle, by using inhibited respiration with a technique such as the active breathing control device, or by delivery of radiation using gating or respiratory correlated CT scanning.
and treatment. Uncertainties from organ motion can also be reduced by using fiducial markers, and published results are available for lung tumors. Radio-opaque markers are inserted and imaged at localization using CT or MRI, and at treatment verification, using portal films, Electronic Portal Imaging Devices (EPIDs) or online cone beam CT Image-Guided Radiotherapy (IGRT). The internal margin therefore allows for inter- and intra-fractional changes in organ position and shape which cannot be expunged.

6.1.5 Treated Volume

This is the volume of tissue that is planned to receive a defined dose and is enclosed by the isodose surface corresponding to that dose level. The shape, size and position of the treated volume in relation to the PTV should be recorded to evaluate and construe local repetitions (in field versus marginal) and complications in healthy tissues, which may be outside the PTV but within the treated volume.

6.1.6 Irradiated Volume

This is the volume of tissue that is radiated to a dose considered notable in terms of healthy tissue tolerance and is dependent on the treatment technique used. The size of the radiated volume relative to the treated volume (and integral dose) may increase with increasing numbers of beams, but both volumes can be reduced by beam shaping and conformal therapy.
6.1.7 Organs At Risk

These are critical healthy tissues whose radiation sensitivity may significantly affect treatment planning and/or prescribed dose. Any movements of the Organs At Risk (OAR) or uncertainties of set-up may be figured with a margin similar to the principles for PTV, to create a Planning organ at Risk Volume (PRV). The size of the margin may diversify in different directions. Where a PTV and PRV are close or overlap, a clinical decision about relative risks of tumor regress or healthy tissue damage must be made. Shielding of parts of normal organs is possible with the use of Multi-Leaf Collimation (MLC). Dose–Volume Histograms (DVHs) are used to calculate normal tissue dose distributions (Fig. 28).

![Diagram of RT planning volumes](image)

Fig. 28. Typical image of RT planning.
6.2 Radiotherapy And Treatment Planning

6.2.1 Radiation And Cell Death

The ionizing radiation causes wide-ranging molecular damage throughout cells by the production of ionized atoms, which cause breakage of chemical bonds, production of free radicals and damage to DNA. Most clinically important effects of radiotherapy are due to irretrievable DNA lesions which result in pasteurization – a loss of proliferative cells’ ability for mislaid cell division. In tumors, loss of proliferative ability by all the cells of the tumor is a necessary condition for tumor cure. Partial sterilization of the tumor cell population results in tumor stasis or regression, giving a clinical remission, followed by regrowth of the tumor from those cells which have retained their proliferative ability. In self-renewing normal tissues, sterilization of proliferative cells leaves the tissues unable to provide replacements for cells that are ordinarily being lost at a consecutive rate from the tissue and introduces a rundown of the mature cells of the tissue. Proliferative sterilization is often referred to as cell kill, with those cells that retain long-term proliferative ability being described as survivors.

6.2.2 Volume Effects

Combined to the total dose and fractionation schedule, target volume is a major variable in radiotherapy. For a given fractionation regimen, higher doses can usually be given when volumes at the same site are small rather than large. Healthy tissues are required to perform orchestrated functions, which can be deteriorated in various ways by radiation. Most normal tissues also cannot regenerate from a single surviving cell. However, tissue recovery may be
helped out by immigration of unirradiated neighboring cells, particularly if the treatment volume is small. Volume is also a significant determinant of normal tissue response to a given dose, first because larger volumes provide less opportunity for tissues to draw on their ‘functional reserve’ and second because larger irradiated volumes make it more likely that a critical volume element will overdraw some upper dose limit. These factors differ according to tissue structure and vary from one treatment to another. In general, the Normal Tissue Complication Probability (NTCP) increases with dose (for a given fractionation regimen) and with the irradiated volume. It is important to know, at least approximately, how changes in irradiated volume at a particular site will affect the tolerance dose which can safely be given. The ‘tolerance dose’ may arbitrarily be defined as that dose which gives no more than 5 per cent incidence of significant side effects, based on clinical experience. A body of data has been amassed which provides some simple ‘rules of thumb’ concerning the trade-off between treatment volume and tolerance dose, but these need to be used very cautiously. Tolerance is affected not only by volume, but also by radiation sensitivity and fraction size, and tolerance to the various new schedules in use must be carefully confirmed by clinical studies. In some cases, radiation injury may result from an excessively high dose to a small tissue element within the treatment volume. The possibility of ensuring better homogeneity of dose dispensation with Intensity Modulated Radiation Therapy (IMRT) may help to meliorate this problem.

6.2.3 Avoidance Of Gaps During Treatment

The occurrence of rapid repopulation in radiated tumors, sometimes with doubling times as short as 3–4 days, has significant implications for interruptions of treatment. Unscheduled gaps occur not infrequently in radiotherapy schedules because of machine breakdown or patient
intercurrent illness or non-attendance. Gaps are significant because they may lead to prolongation of the total treatment time, allowing opportunities for rapid repopulation for surviving tumor cells towards the end of the schedule. Although prolongation will often spare acute healthy tissue reactions, the risk of late effects is not reduced. It has been shown for squamous carcinomas of the head and neck that reductions in cure probability of 1–2 per cent may result from each day of prolongation. If gaps occur, the best management strategy is ‘post-gap acceleration’, i.e. the use of twice daily treatments (separated by more than 6 h) or weekend treatments to enable ‘catching up’ so that treatment is nevertheless completed within the originally intended period. This does not require any changes to fraction size or total dose. However, this approach is not always obtainable in practice. Now that the harmful effect of prolongation is recognized, avoidance of gaps is an important consideration for all radiotherapy departments.

6.2.4 Treatment Scheduling

Radiotherapy schedules have consisted of multiple fractions of 2 Gy delivered for 5 days a week over several weeks. The aggregate dose is usually limited by expected risk of injury to late-responding tissues, although there are situations where acute responses (e.g. mucosal reactions) are the main concern. Treatment schedules with this structure probably take advantage of differences between the survival curves of cells in late-responding tissues (low $\alpha/\beta$ ratio and fraction size sensitivity) and the survival curves of those in typical tumors (with higher $\alpha/\beta$ ratios). This means that late-responding tissues are spared to a greater extent than most tumors by the use of small fractions, giving a propitious therapeutic ratio. Late responses are not strongly influenced by overall treatment time, and it would be desirable to make the
latter as short as possible in order to minimize the opportunities for tumor repopulation. However, this must be balanced by the need to allow time for reoxygenation of hypoxic cells during therapy, and there also may be an adverse effect of reduced treatment time on acute-responding tissues (which also have reduced opportunities for repopulation). All these changes in scheduling may bring important gains in tumor control. However, tumors are known to be extremely heterogeneous with regard to cell survival parameters and growth kinetics, as well as other properties. It is unlikely that any one schedule is ideal for treatment of all tumors, even those of a single pathological type, and it would be highly desirable to select treatment schedules for individual patients on the basis of the radiobiological and kinetic parameters for each tumor. Predictive tests are not yet sufficiently reliable to be used in this way, but individualized scheduling based on biological assay is a likely development for the future.
Chapter 7: Radiation Treatment Parameters

INTRODUCTION

External beam radiotherapy with photon beams is carried out with three types of treatment machines: x-ray units, isotope teletherapy units (mainly cobalt-60 units), and linear accelerators (linacs). The main parameters involved in external beam dose delivery with photon beams are: depth of treatment, field size, source-surface distance in SSD setups or source-axis distance in SAD (isocentric) setups, and photon beam energy. Beams used for radiotherapy have diverse shapes that usually depict a compromise between the actual target shape and the need for simplicity and efficiency in beam shaping. Four general groups of field shapes are used: square, rectangular, circular, and irregular. Square and rectangular fields are usually produced with collimators installed in radiotherapy machines; circular fields with special collimators attached to the treatment machine; and irregular fields with custom-made shielding blocks or with multileaf collimators attached to a treatment machine.

Dose descriptors involved in external beam radiotherapy

7.1 Collimator factor

Exposure in air $X$, air-kerma in air $(K_{air})_{air}$ and “dose to small mass of medium in air” $D'_{med}$ depend on field size $A$ and a parameter referred to as the collimator factor $CF$. The collimator factor is defined as:

$$CF(A,hv) = S_c(A,hv) = \frac{X(A,hv)}{X(10,hv)} = \frac{(K_{air}(A,hv))_{air}}{(K_{air}(10,hv))_{air}} = \frac{D'(A,hv)}{D'(10,hv)}$$
The geometry for the measurement of the collimator factor is shown in part (a) for the measurement of \( D'(A,h\nu) \), in part (b) for the measurement of \( D'(10,h\nu) \) (Fig. 29).

![Diagram of geometry for measurement of collimator factor CF(A,h\nu).]

Fig. 29. Geometry for measurement of collimator factor CF(A,h\nu).

The “dose to small mass of water” is measured at point P in air: in part (a) with field size \( A \), in part (b) with field size \( 10 \times 10 \text{ cm}^2 \).

7.2 Peak scatter factor PSF

The “dose to small mass of medium” \( D'_p \) is measured with just enough material around the point of interest P to provide electronic equilibrium (ionization chamber with appropriate build-up cap). \( D'_p \) is related to \( D_p \), the dose at \( z_{\text{max}} \) in a phantom at point P, through the peak-scatter factor PSF as follows:

\[
PSF(A,h\nu) = \frac{D_p(z_{\text{max}},A,f,h\nu)}{D'_p(A,h\nu)}
\]
With the geometry shown for measurement of $D'_{p}$ in part (a) and measurement of $D_{p}$ in part (b) (Fig. 30). The chamber in part (a) is at a distance of $f+z_{\text{max}}$ from the source.

![Geometry for measurement of peak scatter factor PSF at point P.](image)

**Fig. 30. Geometry for measurement of peak scatter factor PSF at point P.**

### 7.3 Scatter factor $SF$

Scatter factor $SF$ for field $A$ is defined as the ratio:

$$SF(A, hv) = \frac{PSF(A, hv)}{PSF(10, hv)}$$

and thus represents the peak-scatter factor normalized to 1 for a $10 \times 10$ cm$^2$ field (Fig. 31).
7.4 Relative dose factor RDF

For a given photon beam at a given source-surface distance, the dose at point P (at depth $z_{\text{max}}$ in phantom) depends on the field size $A$; the larger the field size, the larger the dose. The relative dose factor RDF is defined as the ratio of $D_P(z_{\text{max}}, A, f, h\nu)$, the dose at P in phantom for field $A$ to $D_P(z_{\text{max}}, 10, f, h\nu)$, the dose at P in phantom for a $10 \times 10$ cm$^2$ field:

$$RDF (A, h\nu) = S_{C,P}(A, h\nu) = \frac{D_P(z_{\text{max}}, A, f, h\nu)}{D_P(z_{\text{max}}, 10, f, h\nu)}$$

The geometry for measurement of the RDF($A, h\nu$) is shown below (Fig. 32). Part (a) for the measurement of $D_P(z_{\text{max}}, A, f, h\nu)$, part (b) for the measurement of $D_P(z_{\text{max}}, 10, f, h\nu)$.
Fig. 32. Geometry for the measurement of the relative dose factor RDF(A). The dose at point P at $z_{\text{max}}$ in phantom is measured with field A in part (a) and with field 10×10 cm$^2$ in part (b).

7.5 Percentage depth dose

Central axis dose distributions inside the patient or phantom are usually normalized to $D_{\text{max}} = 100\%$ at the depth of dose maximum $z_{\text{max}}$ and then referred to as the percentage depth dose distributions.

The percentage depth dose is thus defined as follows:

$$PDD = (d,A,f,hv) = 100 \frac{D_Q}{D_P} = 100 \frac{D_Q}{D_P}$$

Where:

$D_Q$ and $\dot{D}_Q$ are the dose and the dose rate at point Q at depth $z$ on the central axis of the phantom.

$D_P$ and $\dot{D}_P$ are the dose and the dose rate at point P at depth $z_{\text{max}}$ on the central axis of the phantom (Fig. 33).
Fig. 33. Geometry for percentage depth dose measurement and definition.

Point Q is an arbitrary point on the beam central axis at depth d, point P is the point at $z_{\text{max}}$ on the beam central axis. The field size A is defined on the surface of the phantom.

7.6 Scatter function S

In radiation dose calculations it is often desirable to separate the scatter component from the total dose at Q.

\[ \text{Scatter component at } Q = \text{Total dose at } Q - \text{Primary dose at } Q : \]

\[ D'_{p} \ \text{PSF} (A, hv) \ \text{PDD} (z, A, f, hv) - D'_{p} \ \text{PSF} (0, hv) \ \text{PDD} (z, 0, f, hv) \]

The scatter function $S(z, A, f, hv)$ is then defined as:

\[ S(z, A, f, hv) = \text{PSF} (A, hv) \ \text{PDD} (z, A, f, hv) - \text{PSF} (0, hv) \ \text{PDD} (z, 0, f, hv) \]
7.7 Tissue-air ratio

Tissue-air ratio $TAR(z,A_Q, hv)$ was originally introduced to simplify dose calculations in rotational radiotherapy, but its use was subsequently expanded to isocentric irradiations with multiple stationary fields. In rotational radiotherapy the radiation source moves in a circle around the axis of rotation that is usually placed inside the tumor. During the rotation around the patient the SSD varies with the patient contour; however, source-axis distance remains constant.

$TAR(z,A_Q, hv)$ is defined as the ratio of the dose $D_Q$ at point $Q$ on the central axis in the patient or phantom to the dose $D'_Q$, the “dose to small mass of water in air” at the same point $Q$ on the beam central axis:

$$TAR(z,A_Q, hv) = \frac{D_Q}{D'_Q}$$

The geometry for TAR measurement is shown below (Fig. 34). Part (a) for measurement of $D_Q$ in phantom and part (b) for measurement of $D'_Q$ in air. The field size $A_Q$ is defined at point $Q$ that is normally placed into the isocenter of the treatment machine.

---

Fig. 34. Geometry for measurement and definition of tissue-air ratio.
In part (a) the dose is determined at point Q in a water phantom, in part (b) the “dose to small mass of water” is determined at point Q. Point Q is at the machine isocenter at a distance SAD from the source. The beam field size AQ is defined at depth d in the phantom.

- For constant AQ and hv, the TAR decreases with an increasing z beyond z_max.
- For constant z and hv, the TAR increases with increasing AQ.
- For constant z and AQ, the TAR increases with hv.
- For z = z_max, the TAR becomes identical to the PSF:

\[ TAR(z = z_{\text{max}}, A_Q = A_P, hv) = PSF(A_P, hv) \]

The zero area TAR, i.e., TAR(z,0,hv), may be calculated from:

\[ TAR(z,0,hv) = e^{-\mu_{\text{eff}}(z-z_{\text{max}})} \]

where \( \mu_{\text{eff}} \) is the effective attenuation coefficient for the photon beam hv. A 0×0 field is a hypothetical field in which the dose at depth in phantom is entirely due to primary photons since the volume that can scatter radiation is zero.

7.8 Relationship between TAR(d,AQ,hv) and PDD(d,A,f,hv)

As depicted (Fig. 35), a simple relationship may be derived between TAR(z,AQ,hv) and the corresponding PDD(z,A,f,hv) from the basic definitions governing the two functions. The basic definitions for the two functions are:

\[ TAR(z, A_Q, hv) = \frac{D_Q}{D_{1Q}} \]
\[ PDD(z, A, f, hv) = 100 \frac{D_Q}{D_P} \]

And solving these equations for \( D_Q \) we get:

\[ D_Q = D_p \frac{PDD(z, A, f, hv)}{100} = D'_Q \text{TAR}(z, A_Q, hv) \]

\( D_P \) may now be defined as:

\[ D_p = D'_p \text{PSF}(A, hv) = D'_Q \left( \frac{f + z}{f + z_{max}} \right)^2 \text{PSF}(A, hv) \]

And inserted into the equation for \( D_Q \) finally we get:

\[ \text{TAR}(z, A_Q, hv) = \text{PSF}(A, hv) = \frac{PDD(z, A, f, hv)}{100} \left( \frac{f + z}{f + z_{max}} \right)^2 \]

---

Fig. 35. Geometry for the relationship between \( PDD(z, A, f, hv) \) and \( \text{TAR}(z, A_Q, hv) \).
7.9 Scatter-air ratio

Just as it was convenient in dealing with percentage depth doses to separate out the scattered component from the primary component to get the scatter function, it is sometimes useful to separate the primary component of TAR from the total TAR to get the scatter contribution which, in this case, is referred to as the scatter-air ratio SAR\( (d,A_Q,\nu) \). It is defined as:

\[
SAR(z, A_Q, \nu) = TAR(z, A_Q, \nu) - TAR(z, 0, \nu)
\]

Depends on the same three parameters as the TAR, and gives the scatter contribution to the dose at point Q in phantom per 1 cGy of dose to small mass of water at point Q in air.

7.10 Relationship between SAR\( (z,A_Q,\nu) \) and S\( (z,A,f,\nu) \)

Similarly to the relationship between TAR\( (z,A_Q,\nu) \) and PDD\( (z,A,f,\nu) \), we can derive the relationship between SAR\( (z,A_Q,\nu) \) and S\( (d,A,f,\nu) \) to get:

\[
SAR(z, A_Q, \nu) = \frac{S(z,A,f)}{100} \left( \frac{f+z}{f+z_{max}} \right)^2
\]

It is easy to see that:

\[
S(z, A, f, \nu) = 100 \ SAR(z, A_Q, \nu)
\]

for any z when \( f \to \infty \) and for any f when \( z \to z_{max} \).
Chapter 8: Production of Radiation Beam Profiles

INTRODUCTION

Dose distributions along the beam central axis give only part of the information required for an accurate dose description inside the patient. Dose distributions in 2-dimensions and 3-dimensions are determined with central axis data in conjunction with off-axis dose profiles. In the simplest form, the off-axis data are given with beam profiles measured perpendicularly to the beam central axis at a given depth in phantom. Combining a central axis dose distribution with off-axis data results in a volume dose matrix that provides 2-D and 3-D information of the dose distribution (Fig. 36). The off-axis ratio (OAR) is usually defined as the ratio of dose at an off-axis point to the dose on the central beam axis at the same depth in phantom.

Fig. 36. Dose distribution in relation to distance from central axis.
The dose variation across the field at a specific depth is described with the beam profile as shown below (Fig. 37).

Isodose curves are the lines joining the points of equal Percentage Depth Dose (PDD). The curves are usually drawn at regular intervals of absorbed dose and expressed as a percentage of the dose at a reference point.

Isodose charts consist of a family of isodose curves. The depth dose values of the curves are normalized: at the point of maximum dose on the central axis ($D_{\text{max}}$), at a fixed distance along the central axis in the irradiated medium (SAD). The sources of an isodose chart are the following: Atlas of pre-measured isodose charts, it can be generated by calculations using plenty of algorithms for treatment planning and finally the manufacturers of radiation generators (Fig. 38).
Fig. 38. *Isodose charts in SSD & SAD setup.*

8.1 Parameters of isodose curves

The parameters that react on the single beam isodose distribution are: the beam quality, source size, SSD and SAD, the penumbra effect, collimation and flattening filter, and field size. Regarding beam quality, the depth of a given isodose curve increases with beam quality. Greater lateral scatter is associated with low-energy beams. For megavoltage beams, the scatter outside the field is minimized as a result of forward scattering and becomes more a function of collimation than energy. One of the most important parameters in treatment planning is the field size (Fig. 39).
More specifically, the field size is smaller than 6 cm. It has relatively a large penumbra region and a bell shape. Thus TPS should be mandatory for small field size.

8.2 Collimation and flattening filters

Isodose curves are lines that join points of equal dose. They offer a schematic representation of the dose distribution and show the behavior of the beam or the combination of beams with different wedges, bolus and shielding. In current time, there are three types of wedge filters: manual, motorized and dynamic. Physical wedges are angled pieces of lead or steel that are placed in the beam to produce a gradient in radiation intensity. Manual intervention is required to set the physical wedges on the treatment unit’s collimator assembly. A motorized wedge is
a physical wedge integrated into the head of the unit and controlled remotely. Last but not least, a dynamic wedge produces the same wedged intensity gradient by having one jaw close gradually while the beam is on. Bolus is a tissue-equivalent material placed in contact with the skin to manage one or both of the following: (a) to increase the surface dose and (b) to remunerate for missing tissue. On the other hand, isodose curves are used to evaluate treatment plans along a single plane or over several planes in the patient. The isodose covering of the target periphery is compared to the isodose at the isocentre. If the ratio is within a desired range (e.g., 95-100%) then the plan may be receivable provided critical organ doses are not overdrew. This approach is ideal if the number of transversal slices is small.

Therefore, another important parameter in treatment planning is the collimation and flattening filter. The collimation filter consists of: the collimator block, the flattening filter, the absorbers and scatters. The flattening filter has the greatest influence in determining the shape of the isodose curves. The photon spectrum may different for the peripheral areas compared with the central part of the beam. Last but not least, the change in quality across the beam causes the flatness to change with depth. Finally, another parameter in treatment planning are the wedge filters (Fig. 40). A beam modifying device, which causes a progressive decrease in intensity across the beam, resulting in tilting the isodose curves to the thinner side. Wedge filters are most commonly made of tungsten, brass, lead or steel (Fig. 41).
Fig. 40. Various blocks and wedge filters.

**Individual wedge system**

- A separate wedge for each beam width.
- To minimize the loss of beam output.
- To align the thin end of the wedge with the border of the light field
- Used in cobalt-60 teletherapy machine.

**Universal wedge system**

a. A single wedge for all beam width.

b. Fixed centrally in the beam.

c. Used in Linear Accelerator.

Fig. 41. Schematic Representation of various wedge filters.
Chapter 9: Treatment Planning Radiation Fields

INTRODUCTION

External photon beam radiotherapy is usually carried out with multiple radiation beams in order to accomplish a uniform dose distribution inside the target volume and a dose as low as possible in healthy tissues surrounding the target. It is almost a rule strict enough, in external beam radiotherapy: Successful radiotherapy requires a uniform dose distribution within the target (tumor).

9.1 The external photon beam radiotherapy

International Commission on Radiation Units and Measurements (ICRU) set forth recommendations regarding dose uniformity, prescribing, recording, and reporting photon beam therapy. The ICRU report 50 recommends a target uniformity of dosage units within +7 % and –5 % relative to the dose delivered to a well-defined prescription point within the target (tumor) (Fig. 42). To achieve this goal contemporaneous external photon beam radiotherapy is performed with a diversity of beam energies and field sizes.

Fig. 42. Percentage of dose delivered as a function of penetration depth.
Beam energies used:

• Superficial (30 kV to 80 kV)

• Orthovoltage (100 kV to 300 kV)

• Megavoltage or supervoltage energies (Co-60 to 25 MV)

Several field sizes are shown below in Fig. 43, 44 and 45:

Fig. 43. Small circular fields used in radiosurgery.

Fig. 44. Standard rectangular and irregular fields.
9.2 The setup convention types

Photon beam radiotherapy is carried out under two setup conventions: constant Source-Surface Distance (SSD technique) and isocentric setup with a constant Source-Axis Distance (SAD technique). Regarding of SSD technique it is carried out while the distance from the source to the surface of the patient is kept constant for all beams. The production of the radiation beam fields aimed at radiotherapy is being performed by especially evolved software (Fig. 46, 47).
On the other hand, as far as it is concerned the SAD technique is accomplished while the center of the target volume is placed at the machine isocenter, i.e. the distance to the target point is kept constant for all beams.

Fig. 47. Production of the radiation beam fields in an SAD technique.

In contrast to SSD technique, the SAD technique requires no adjustment of the patient setup when turning the gantry to the next field. The process of determining the volume for the treatment of a malignant disease consists of several distinct steps. In this process, different volumes may be defined, e.g. due to: varying concentrations of malignant cells, probable changes in the spatial relationship between volume and beam during therapy, movement of patient, possible inaccuracies in the treatment setup. The following figure (Fig. 48) describe these "ICRU volumes" that have been defined as principal volumes related to three dimensional treatment planning.
9.3 The essentials of radiotherapy prescription

The complete prescription of radiation treatment must include: definition of the aim of therapy, volumes to be considered, prescription of dose and fractionation. Only detailed information regarding total dose, fractional dose and total elapsed treatment days allows for proper comparison of outcome results. Different concepts have been developed for this requirement. The ICRU report 50 recommends a target dose uniformity within +7 % and –5 % relative to the dose delivered to a well-defined prescription point within the target. Since some dose heterogeneity is always present, a method to describe this dose heterogeneity within the defined volumes is required. ICRU Report 50 is suggesting several methods for the representation of a spatial dose distribution. Parameters to characterize the dose distribution within a volume and to specify the dose are: minimum target dose, maximum target dose, mean target dose, a
The ICRU has given recommendations for the selection of a representative point (the so-called ICRU reference point). The ICRU reference dose point is located at a point chosen to represent the delivered dose using the following criteria: the point should be located in a region where the dose can be calculated accurately (i.e., no build-up or steep gradients), the point should be in the central part of the PTV, for multiple fields, the isocenter (or beam intersection point) is recommended as the ICRU reference point. Specific recommendations are made with regard to the position of the ICRU (reference) point for particular beam combinations: for single beam, the point on central axis at the center of the target volume, for parallel-opposed equally weighted beams, the point on the central axis midway between the beam entrance points, for parallel-opposed unequally weighted beams, the point on the central axis at the center of the target volume, for other combinations of intersecting beams, the point at the intersection of the central axes (insofar as there is no dose gradient at this point). Within the simulation process of the entire treatment using the computerized treatment planning system, the patient anatomy and tumor targets can be represented as three dimensional models (Fig. 49).

Fig. 49. 3-D computerized treatment planning simulation process. CTV (Clinical Target Volume): Mediastinum (violet). OAR (Organs At Risk): Lungs (yellow), spinal cord (green).
The patient information required for treatment planning in particular depends on whether the system used is 3-D as above or 2-D as shown below (Fig. 50).

![Fig. 50. 2-D treatment planning simulation process.](image)

On the one hand, regarding of 2-D treatment planning is a single patient contour, acquired using lead wire or plaster strips, is transcribed onto a sheet of graph paper, with reference points identified. Simulation radiographs are taken for comparison with port films during treatment. For irregular field calculations, points of interest can be identified on a simulation radiograph, and SSDs and depths of interest can be determined at simulation. Organs at risk can be identified and their depths determined on simulator radiographs. On the other hand, the 3-D treatment planning is a CT dataset of the region to be treated is required with a suitable slice spacing (typically 0.5 - 1 cm for thorax, 0.5 cm for pelvis, 0.3 cm for head and neck). An external contour (representative of the skin or immobilization mask) must be drawn on every CT slice used for treatment planning. Tumor and target volumes are usually drawn on CT slices. Organs at risk and other structures should be drawn in their entirety, if dose-volume histograms are to be calculated. MRI or other studies (PET) are required for image fusion. With many
treatment planning systems, the user can choose: to ignore inhomogeneities (often referred to as heterogeneities), to perform bulk corrections on outlined organs, to use the CT data itself (with an appropriate conversion to electron density) for point-to-point correction. CT images can be used to produce Digitally Reconstructed Radiographs (DRRs). DRRs are used for comparison with portal films or beam’s eye view to verify patient set up and beam arrangement. Patient simulation was initially developed to ensure that the beams used for treatment were correctly chosen and properly aimed at the intended target. Presently, treatment simulation has a more expanded role in the treatment of patients consisting of: determination of patient treatment position, identification of the target volumes and OARs, determination and verification of treatment field geometry, generation of simulation radiographs for each treatment beam for comparison with treatment port films, acquisition of patient data for treatment planning.

9.4 The types of image simulation

Comparison of simple simulation with portal image (MV) and conventional simulation with diagnostic radiography (kV) of the same anatomical site (prostate) demonstrates the higher quality of information on anatomical structures (Fig. 51).

Check portal film (MV). Reference simulator film (kV).

Fig. 51. Comparison of simple simulation with portal image (MV) and conventional simulation with diagnostic radiography (kV).
It is neither efficient nor practical to perform simulations with portal imaging on treatment units. There is always heavy demand for the use of treatment units for actual patient treatment. Using them for simulation is therefore considered an inefficient use of resources. These machines operate in the megavoltage range of energies and therefore do not provide adequate quality radiographs for a proper treatment simulation. Thus, there is poor image quality. Reasons for the poor quality of port films: most photon interactions with biological material in the megavoltage energy range are Compton interactions that produce scattered photons that reduce contrast and blur the image. The large size of the radiation source (either focal spot for a linear accelerator or the diameter of radioactive source in an isotope unit) increases the detrimental effects of beam penumbra on the image quality. Patient motion during the relatively long exposures required and the limitations on radiographic technique also contribute to poor image quality. Therefore, dedicated equipment – fluoroscopic simulator - has been developed and was widely used for radiotherapy simulation (Fig. 52).

Fig. 52. Typical image of a dedicated fluoroscopic simulator.
Modern simulation systems are based on computed tomography (CT) or magnetic resonance imagers (MRI) and are referred to as CT simulators or MRI simulators (Fig. 53).

Fig. 53. Typical image of a dedicated radiotherapy CT simulator.
Conclusions

Lung cancer is one of the most lethal types of cancer. It affects a life-sustaining system of the body, the respiratory system. The more we learn about lung cancer the more we will be able to take efficient decisions about someone’s treatment and aftercare. Lung cancer explicates when normal lung cells maintain genetic damage that ultimately leads to uncontrolled cell multiplication. Lung cancer is divided into two main types based on how it looks under the microscope: Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC). They have different patterns of growth and spread and are also treated differently. Most people diagnosed with lung cancer present symptoms related to the fatal disease but they occur late in the disease process. This silent growth of lung cancer has led scientists to develop various diagnostic methods. Lung cancer is currently cured by three forms of treatment. These are: surgery, chemotherapy and radiotherapy. They are used on the patient in combination or separately depending on the type of lung cancer from which he or she suffers and the stage of illness. In this thesis we focus on the subject of radiation therapy for lung cancer. The machine that allows us to perform radiotherapy is the medical linear accelerator among others. The practice of radiotherapy requires some factors contributing to planning radiotherapy treatment. External beam radiotherapy with photon beams is carried out with three types of treatment machines: x-ray units, isotope teletherapy units (mainly cobalt-60 units), and linear accelerators (linacs). The main parameters involved in external beam dose delivery with photon beams are: depth of treatment, field size, source-surface distance in SSD setups or source-axis distance in SAD (isocentric) setups, and photon beam energy.
# LIST OF ABBREVIATIONS AND ACRONYMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACS</td>
<td>American Cancer Society</td>
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<tr>
<td>CAD</td>
<td>Computer-Assisted Diagnosis</td>
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<td>CEA</td>
<td>Carcinoembryonic Antigen</td>
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<td>CF</td>
<td>Collimator Factor</td>
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<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<tr>
<td>CT</td>
<td>Computerized Tomography</td>
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<tr>
<td>CTV</td>
<td>Clinical Target Volume</td>
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<tr>
<td>DHC</td>
<td>Dihydrocodeine</td>
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<tr>
<td>DNA</td>
<td>DeoxyriboNucleic Acid</td>
</tr>
<tr>
<td>DRRs</td>
<td>Digitally Reconstructed Radiographs</td>
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<tr>
<td>DVHs</td>
<td>Dose–Volume Histograms</td>
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<tr>
<td>EPIDs</td>
<td>Electronic Portal Imaging Devices</td>
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<tr>
<td>FNA</td>
<td>Fine Needle Aspiration</td>
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<tr>
<td>GTV</td>
<td>Gross Tumor Volume</td>
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<tr>
<td>ICRU</td>
<td>International Commission on Radiation Units</td>
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<tr>
<td>IGRT</td>
<td>Image Guided Radiation Therapy</td>
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<td>IMRT</td>
<td>Intensity-Modulated Radiation Therapy</td>
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<tr>
<td>LCC</td>
<td>Large Cell Carcinoma</td>
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<tr>
<td>LINAC</td>
<td>Linear Particle Accelerator</td>
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</table>
MLC - Multi-Leaf Collimation
MRI - Magnetic Resonance Imaging
NSCLC - Non-Small Cell Lung Cancer
NTCP - Normal Tissue Complication Probability
OAR - Off-Axis Ratio
OAR - Organs At Risk
PDD - Percentage Depth Dose
PET - Positron Emission Tomography
PRV - Planning organ at Risk Volume
PSA - Prostate Specific Antigen
PSF - Peak Scatter Factor
PTV - Planning Target Volume
RDF - Relative Dose Factor
RT - Radiation Therapy
SAD - Source-Axis Distance
SAR - Scatter Air Ratio
SBRT - Stereotactic Body Radio Therapy
SCC - Squamous Cell Carcinoma
SCLC - Small Cell Lung Cancer
SF - Scatter Factor
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>SRS</td>
<td>Stereotactic Radiosurgery</td>
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<tr>
<td>SSD</td>
<td>Source-Surface Distance</td>
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<tr>
<td>TAR</td>
<td>Tissue Air Ratio</td>
</tr>
<tr>
<td>TNM</td>
<td>Tumor characteristics including size, location, and local invasion, regional lymph node involvement, Metastasis status</td>
</tr>
<tr>
<td>TPS</td>
<td>Treatment Planning System</td>
</tr>
<tr>
<td>VATS</td>
<td>Video-Assisted Thoracoscopy</td>
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<td>VMAT</td>
<td>Volumetric Modulated Arc Therapy</td>
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<td>WHO</td>
<td>World Health Organization</td>
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