Chapter 1

Introduction

This chapter describes the general information on cancer, types of cancer, histology, pathology, biochemistry, radiation effects on cancer. It also deals with physical, chemical and surgical approaches to the treatment of cancer. Survey of literature on pathological, biochemical, histological and radiation aspects on cancer are dealt with. Finally, the genesis of the present investigation is mentioned.
Cancer is an abnormal, continuous multiplying of cells. The cells divide uncontrollably and may grow into adjacent tissue or spread to distant parts of the body. The mass of cancer cells become large enough to produce tumors that can be detected.

The cancer cells can be benign or malignant: Some cancers, such as leukemia, start in the blood and blood-forming organs and do not form tumors. Instead, these cancer cells circulate through other tissues where they grow. Treatments for cancer focus on stopping this growth by killing cancer cells while causing as little damage as possible to surrounding normal cells.

Different kinds of cancer start in different areas of the body. These illnesses respond differently to treatment. The human body is made of more than 200 different types of living cells. Cancer can start in any of these cell types. There are more than 200 types of cancer.

Each cancer starts with changes in one cell or a small group of cells. The cells have started to reproduce uncontrollably many years before a lump is felt or a doctor sees it on a scan. The differences between normal cells and cancer cells are that the cancer cell seems to lose a number of vital control systems. This is due to some of the genes in the cell having been damaged or lost. This is known as mutation.
1.1. What is cancer?

Cancer is a term covering all malignant tumourous formations whose kinds total over 100 and includes fast killing sarcomas of the non osteous tissue and slow chronic disorders of the lymphatic system in which remissions and temporary improvements may occur. Carcinogenesis is a multi stage process in which a benign tissue may become malignant.

The most important properties of malignant tissues are run away multiplication of cells which have gone out of control by the host organism, the ability to penetrate or to grow into healthy tissues and cause functional disorders and damage there, the ability to break away from the bulk of the tumour and proliferate with the blood stream into other organs and tissues and form metastasis or secondary tumours, the ability to cause overall metabolic disorders and poison the organism with the decay products of the tumour cells.

Cancer is also treacherous in the infinite variety of cancer aggravating and inducing factors, Search for common patterns in their action is also high on the research agenda.
1.2. Types of cancers

Cancers are classified on the basis of their location or the body site from which they arise.

**Carcinomas:** These cancers are located in the epithelial lining of internal organs or glands. For e.g., Breast cancer, Stomach cancer etc., Cancers of epithelial glands are called Adenoma. About 85% of all tumours are of this kind.

**Melanomas:** These are cancerous growths of melanocytes (skin cells).

**Sarcomas:** These cancers are located in connective and muscular tissues. These are derived from tissues of mesodermal origin that is bone, fat and cartilage. If cancer affects the Lymphatic system, it is called Lymphomas.

**Leukaemia** (Blood cancer): These are characterized by increased WBC count of the blood (up to 2,00,000 - 1000,000/mm³) due to their increased production in the bone marrow.

**Myeloma:** These are malignant tumours occurring in middle aged and older people. It interferes with the blood cell producing function of bone marrow and cause anaemia.

Cancer cells can break away from the primary tumour and be carried in the blood or lymphatic system to other parts of the body where
they can start to grow into new tumours. Tumours from cancers that have spread are called 'secondary cancers' or 'metastases'.

The various organs of the body are made up of different types of cells. Any of these cell types can grow into a primary cancer. Different types of cancer behave very differently.

The cancer incidence is around 120/100000 per year in India compared to 300/100000 per year in the world. Every year about 8,50,000 new cancer cases are diagnosed in India resulting in about 5,80,000 cancer related deaths every year.

India has the highest number of the oral and throat cancer cases in the world. Every third oral cancer patient in the world is from India. Oral, lung and stomach cancers are the three most common causes of cancer incidence and death among males. In females, cervix, breast and oral cancers are the three main causes of cancer related illnesses and death.

Compared to developed countries overall there are less cancer cases in India but this could be due to un-diagnosed and un-reported ones. At the same time regional, ethnic, dietary factors might also results in difference in the cancer susceptibilities and the incidence.
1.3. Histology of cancer

Histology is the study of tissues and cells under a microscope. There are four phases which can be seen in cancer: Transformation of a single cell, called the target cell, the transformed cell has a selective and growth advantage over its surrounding cells and begins to grow, growth exceeds its confines and local invasion begins and finally distant metastases will develop. The cancer cell looses a number of vital control systems. This is due to the loss or damage of some cells on the genes.

Tumor biology kinetics

Malignant cancers usually show evidence of increased mitotic activity. They do not always multiply faster than their normal counterparts. However a tumour results because of an imbalance between cellular proliferation and cell loss. Malignant cells like normal cells have a finite life span.

A variable proportion of cells within a tumour is malignant and there is often a substantial component of non malignant reactive cells. Only a proportion of the malignant cells within a cancer has a capacity for indefinite cell self replication. These are known as stem cells and are the targets for treatment with radiotherapy or drugs.

The proportion of these cells proceeding through the cell cycle to mitosis at any one time is known as the growth fraction. The remainder
of the malignant cells is in a resting phase and can be recruited into
growth fraction which is sometimes very small but in some rapidly
growing tumours it can approach 100% of the total malignant cell
population.

The rate of tumour growth depends on the size of the growth
fraction and also on the cell cycle time i.e., the time from one mitosis to
the next. The great variations in cellular proliferation and loss account
for the very large variations in tumour doubling time which can vary
from few days to few years. Initially the rate of cellular proliferation leads
to approximately exponential tumour growth. But the rate falls due to
reduction in the blood supply to individual cells as the tumour enlarges.

**Heterogeneity**

Most cancers arise from one mutation in a single cell and so
represent monoclonal proliferation although further mutations are
inevitable as the tumour grows. There are approximately $10^9$ cells within
one cubic cm of a tissue. And most cancers are substantially larger than
this when detected.

Thus most cancers are to some extent heterogenous. Manifestation
of heterogeneity includes variations in cellular appearance, hormone
receptor concentrations and variations in the response to treatment in
different metastasis. Radiotherapy, hormone therapy, chemotherapy
often fails because of the presence of small number of cells which are resistant to attack.

**Invasion.**

The hallmark of malignant tumour is the ability to invade locally and spread to different sites. Local invasion is often much more extensive. Malignant tumours do not form capsules although compression of the surrounding tissue may occasionally create a false capsule. This is common in soft tissue sarcomas. For example mere shelling out will almost fail to remove all the malignant cells.

**Metastasis.**

Metastatic spread is complicated process which occurs more frequently with undifferentiated, rapidly growing tumours. Only a very small proportion of shed cells are capable of eventual development into overt distant tumours. For a successful hematogenous spread, cells have to breach the vascular basement membrane within the primary tumour, survive transport in the blood stream, breach the basement membrane in a target organ and then proliferate in a foreign micro environment.

The characteristics of the micro environment are crucial for the above process. The distribution of the blood born metastasis does not closely reflect the blood flow to different sites. Some primary carcinomas may remain hidden even in the presence of enormous blood born or
lymphatic metastasis. The principle route for metastasis is via blood and lymphatic vessels. Only lung tumours have direct access to the arterial system. For other tumours arterial spread can occur only after shed cells have successfully negotiated the lungs or have established lung metastasis.

As the tumour gets bigger, the centre of the tumour gets less and less of the oxygen and the other nutrients that all cells need to survive since the cells are far away from blood vessels. Cancer at the very early stage is called ‘carcinoma in situ’. This means that it is very small and hasn’t spread to anywhere in the body.

These cancers are so small that they will not be found unless they are in accessible sites such as skin, cervix etc., A carcinoma in situ in an internal organ cannot be subjected to scanning. The exceptions are breast cancer and cervical cancer. Both can be picked up through mammograms and cervical smears.

Normal cells can cause stimulation for the growth of new blood vessels. This happens at the time of repairing the damaged tissue. This is called angiogenesis. Normal cells produce proteins such as angiogenic and antiangiogenic factors which can help the growth of blood vessels on and off respectively.
Angiogenesis plays an important part in cancer spread. The newly developing capillary cells release substances that help the cancer cells to detach from the primary tumour and get into the bloodstream. This means that the cells can travel to another part of the body and begin to grow there.

The angiogenic factors are available plenty at the outer edges of a tumour. Anti-angiogenic drugs may stop a cancer from growing into surrounding tissue or spreading. They will probably not be able to get rid of a cancer, but may be able to shrink it or stop it growing in some cases.

Some anti-angiogenic drugs can control some types of cancer. Examples of drugs that interfere with blood vessel growth are Interferon alpha, Thalidomide and Bevacizumab (Avastin). As the tumour grows and takes up more space, it begins to press on the normal body tissue nearby. The tumour growth will force itself through the normal tissue.

As the cancer grows, it will squeeze and block small blood vessels in the area. Due to low blood and oxygen levels, some of the normal tissue will begin to die. This makes the tumour to continue its way through. Normal blood cells produce enzymes and the blood cells use them to attack bacteria and viruses.

Many tumours contain this kind of enzymes in larger numbers than in normal tissues. Cancerous cells make those enzymes and give
them out into the blood stream or tissues. Growing tumours have high levels of enzymes that break down tissue. These enzymes make it easier for the tumour to make a pathway for itself into the normal tissue.

1.4. Pathology of cancer

Pathology is a broad and complex scientific field to understand the mechanisms of injury to cells and tissues, as well as the body’s means of responding to and repairing injury.

Changes in the DNA of the body cells are known as somatic mutations. A mutation arises in the egg or a sperm is known as germ line mutations and will normally be present in the body cells so that they can be passed on to the next generation. Most mutations are likely to impair the survival of all dividing cells resulting new clone will die out.

In cancer we are concerned with those mutations that lead to uncontrolled division. A single mutation is not generally sufficient to cause cancer. Two or more genetic changes are required for the development of the cancer. A class of cancer inducing genes, cellular oncogenes is the normal genes which have been altered in a way that makes them function inappropriately.

Various mutational mechanisms may be identified. Chromosome trans locations, point mutations, deletions, insertions, gene amplification and retro viral transduction. These genes act dominantly. Only one of the
pair needs to be altered to produce the effect. And their mutations have not so far been found to be passed from generation to generation and hence not to contribute to familial cancer susceptibility.

The diagnosis of specific type of cancer is made by the identification of certain pathological features such as presence of melanin pigment in malignant melanoma.

Squamous cell carcinoma of lung, larynx, skin and oesophagus are identified by the presence of keratin pearls in well differentiated examples. Adenocarcinoma in stomach, bowel, lungs and breast show gland formation if well differentiated. Sarcomas are usually composed of long spindle shaped cells. Glycogen is abundant in such cells.

Malignant lymphomas are divided into Hodgkins disease and non Hodgkins disease. The diagnosis of hodgkins disease depends on the detection of specific cell type having a bi lobed nucleus. In non hogdkins lymphomas the immunocytochemistry can be used to identify malignant lymphomas.

A cancer may be suspected for a variety of reasons, but the definitive diagnosis of most malignacies must be confirmed by histological examination of the cancerous cells by a pathologist. Tissue can be obtained from a biopsy or surgery. The tissue diagnosis given by the pathologist indicates the type of proliferating cells, its histological
grade, genetic abnormalities, and other features of the tumor. Together, this information is useful to evaluate the prognosis of the patient and to choose the best treatment. Cytogenesis and immunohistochemistry are other types of testing on the tissue specimen.

A pathologist will encounter metastasis in a variety of situations when examining a specimen. The lymph nodes may be sampled to detect secondaries: with carcinoma of colon the nodes in the pericolic fat are observed, whereas with breast carcinoma, axillary lymph nodes must be observed.

In fact when examining any tumour, the possibility of metastatic disease must always be considered and the distinction of primary and secondary malignancies is a major part of the histopathological diagnosis of the cancer.

These tests may provide information about the molecular changes (such as mutations, fusion genes, and numerical chromosome changes) in the cancer cells, and indicate the future behavior of the cancer (prognosis) and best treatment.

1.5. Biochemistry of cancer

Study of the chemical phenomena in living organisms is called biochemistry. Proteins, carbohydrates, lipids, nucleic acids and other
Biomolecules are studied in detail under this branch including the structure and functions.

Biochemistry studies the chemical properties of important biological molecules, like proteins, and in particular the chemistry of enzyme-catalyzed reactions. Other areas of biochemistry include the genetic code (DNA, RNA), protein synthesis, cell membrane transport, and signal transduction. The biochemical differences between normal and malignant cells were discovered in their patterns of enzymatic activity.

Glycolysis in human and animal tumors has an increased rate. It was noticed that when normal tissue slices were incubated in a nutrient medium containing glucose, in the absence of oxygen have produced lot of lactic acid but in the presence of oxygen the production of lactic acid reduced.

It is concluded that cancer cells undergo a damage in the presence of oxygen to their respiratory mechanism confirms the increase in the rate of lactic acid production in the presence of oxygen. The persistence of this type of glycolysis is the important biochemical lesion in neoplastic transformation. This idea has some importance to come to a conclusion that anaerobic metabolism predominates in the hypoxic areas in the centre of tumors.
“Convergence hypothesis” of cancer was formulated by Greenstein. It states that malignant neoplasm exhibit the enzymatic activity to converge to a common pattern. Even though cancer cells have the commonly increased metabolic pathways, there is tremendous biochemical heterogeneity among malignant neoplasm.

Millers studied the “deletion hypothesis” of producing hepatic cancer by feeding aminoazo dyes. This resulted a carcinogenic aminoazo dye covalently got bound to liver proteins undergoing carcinogenesis in animals whereas no dye binding has occurred with the protein of tumors which were induced by the dye. Carcinogenesis resulted a permanent alteration or loss of protein essential for the control of growth.

According to Potter, the proteins lost during carcinogenesis may be involved in the feedback control of enzyme systems required for cell division, and he proposed the feedback deletion hypothesis and postulated that “repressors” are important in the regulation of genes involved in cell multiplication are lost by monogenic agents on the cell, either by interacting with DNA to block repressor gene transcription or by reacting directly with repressor proteins and inactivating them.

This prediction anticipated the discovery of tumor suppressor proteins, such as p53 and RB. For example pyrimidine and purine synthesis has increased the changes in cancer cells whereas pyrimidine
and purine catabolism has decreased the variation in cancer genes. RNA and DNA synthesis has increased the variation in tumour cells. Glucose catabolism and synthesis have increased and decreased the alterations in cancer cells respectively. Amino acid catabolism has decreased the changes in cancer cells.

The enzyme patterns of cancer cells indicate undifferentiated and highly malignant cells resemble one another whereas fetal tissues have more than their adult normal counterpart cells and also well-differentiated tumors resemble in their cell of origin more than other tumors. This heterogeneity exists for tumors of the same tissue type in different patients and for the same patient at different stages of the disease.

Chemicals cause genetic damage in different ways namely the formation of carcinogen DNA adducts, leading to a base mutation or gross chromosomal changes. Adducts are formed when mutagen or a part of it irreversibly bonded to DNA so that it can cause a base substitution, insertion, deletion during DNA replication.

Gross chromosomal mutations are chromosome breaks or gaps. The level of DNA damage is the biologically effective dose in a target organ and reflex in a net result of carcinogen exposure activation, lack of detoxification, lack of DNA repair and lack of programmed cell death.
People are commonly exposed to N-nitrosamines and other N-nitro so compounds from dietary and tobacco exposures which are associated with DNA adduct and formation of cancer. Polycyclic aromatic hydrocarbons are associated with lung, breast and oral cavity cancers. Benzene leads to leukemia.

Several ectopic hormones are also produced by different types of cancers in human beings. For example carcinoma of lung, pancreas, thyroid, prostate, ovary and cervix produce adenocorticotropin hormone. Carcinomas of lung, breast, prostate, bladder, pancreas, Liver, esophagus, stomach, colon, larynx, testis, carcinoid tumors, insulinoma, melanoma lead to the production of anti-diuretic hormone.


### 1.6. Radiation effects on cancer

Certain type ionizing radiations kill cancer cells and shrink tumors and this is called Radiation therapy. Radiation therapy destroys cells in the area being treated by damaging their DNA, making it impossible for
cells to continue to grow and divide. Although radiation damages both cancer cells and normal cells, most normal cells can recover from the effects of radiation and function properly. The goal of radiation therapy is to damage as many cancer cells as possible, while limiting harm to nearby healthy tissue.

One of the most important cellular functions affected by radiation is the ability of the cell to divide and produce a line of progeny. If a cell retains such an ability following irradiation, it is said to have survived. The survival of cells after radiation treatment has been studied extensively because of its importance in cancer therapy.

Because radiation treatment is usually given in a series of daily doses spread over a number of weeks, the four factors that influence the effect of such fractionated treatment are repair of sublethal damage, repopulation by surviving cells in the irradiated tissues, redistribution of cells throughout the cell division cycle and reoxygenation of hypoxic cells, primarily in tumours.

The effects of radiation on tissue as a function of dose are measured with assays and the measurement results are given in the form of cell survival curves or dose response curves. Clonogenic assays measure the reproductive integrity of the clonogenic stem cells in tissue.
Functional assays measure functional end points for various tissues and produce dose response curves in which the response is expressed as a proportion of cases in which reactions are greater than a specified level. Lethality assays quantify the number of animal death after irradiation of the whole animal or of a specific organ with a given dose. The deduced parameter LD50 stands for lethal dose, defined as the dose to animals or to a specific organ of animals that kills 50% of the animals.

The aim of radiotherapy is to deliver enough radiation to the tumour to destroy it without irradiating normal tissue to a dose that will lead to serious complications. The optimum choice of radiation dose delivery technique in the treatment of a given tumour is such that it maximizes the tumour control probability (TCP) and simultaneously minimizes the normal tissue complication probability (NTCP).

In reality tumours are more heterogeneous than normal tissues. It is imperative that the average doses to normal tissues be kept lower than the dose to tumours in order to minimize treatment complications and optimize treatment outcomes. In modern radiotherapy this is achieved through sophisticated 3-D treatment planning and dose delivery. The therapeutic ratio varies with many factors such as the dose rate and LET of radiation, the presence of radiosensitizers or radioprotectors, the
design of the treatment plan and the precision of implementation of the treatment plan.

The sensitivity of cells is dependent on many factors. One such factor is the position of the cell in its proliferation cycle. The cell cycle is marked by two well defined portions. Mitosis M, where division takes place and the period of DNA synthesis.

The S and M portions of the cell cycle are separated by two periods G1 and G2 where DNA is not synthesized but other metabolic process continue. For mammalian cells the S phase is usually 6-8 hours, M less than an hour, G2 in the range 2-4 hours and G1 lasting for 1-8 hours. The total cell cycle time is usually 10-20 hours.

In a growing cell population the constituent cells will be asynchronously distributed through all phases of the cell cycle. Because of the cell-age-specific radiosensitivity, an asynchronous cell population will be partially synchronized by irradiation since those cells in the sensitive portions of the cycle will have a lower probability of survival than those in the resistant phases. Thus when an asynchronous cell population is irradiated, the surviving cells will be partially synchronized into the resistant phase.
As these cells progress through the cell cycle they will move into the more sensitive phases. As a cell population continues to grow following irradiation, the partially synchronized surviving cells are rapidly redistributed throughout the cell cycle with the result that the cell population will again contain some cells in sensitive phases. This process of redistribution in proliferating cell population will thus tend to increase the cell kill from fractionated treatment relative to that from a single dose. Such an effect will not occur in nonproliferating cell populations.

Radiation has been used to treat patients with cancer, fractionating the radiation treatment given over a period of weeks, resulting in a better therapeutic ratio for most tumours than giving the treatment as a single dose. When radiation treatment is fractionated it is found that a much greater total dose is required to achieve a given level of biological damage than when a single dose is used. This indicates that recovery from the radiation damage occurs between fractions.

This recovery is a complex process involving repair of damage by individual cells and the effects of cell growth during the fractionated course of treatment. Mammalian cells can repair sublethal radiation damage by a variety of enzymes and pathways. When a radiation treatment is fractionated over 4 to 6 weeks, the cells in the treated area
may proliferate during the course of treatment. The presence of oxygen at the time of irradiation acts as a sensitizing agent.

The biological effects of radiation are greater in the presence of oxygen than in its absence. Cells at the periphery of tumour cords growing around blood vessels become chronically hypoxic because of the consumption of most of the oxygen near the blood vessel. The transient closing of blood vessels can also make the whole tumour cord hypoxic for a few minutes at a time. Reoxygenation is the process by which cells that are hypoxic become oxygenated after irradiation, through the killing and removal of oxic radiosensitive cells from the tumour.

Division of dose into multiple fractions spares normal tissues through repair of sublethal damage between dose fractions and repopulation of cells. The former is greater for late reacting tissues and the latter for early reacting tissues. Concurrently, fractionation increases tumour damage through reoxygenation and redistribution of tumour cells.

A balance is achieved between the responses of tumour and early and late reacting normal tissues, so that small doses per fraction spare late reactions preferentially and reasonable schedule duration allows regeneration of early reacting tissues and tumour reoxygenation to likely
occur. The current standard fractionation is based on five daily treatments per week and a total treatment time of several weeks.

Radio therapy involves the use of ionizing radiation to treat cancer. The radiation used is of very high energy and short wave length. Ionizing radiation is capable of displacing electrons from their orbit around the nucleus of atoms. This creates instability and the free electron is captured by nearby atoms which also become unstable because of their additional negative charge. When living tissue is exposed to ionizing radiation cellular destruction can be initiated.

The radiation sensitivity of the tissue or tumor therefore depends both on the amount of damage sustained by its cells and their stability to repair sub lethal damage. There is a wide radiation sensitivity of normal tissues and tumor. Even within a tumor, sensitivity may vary depending on the oxygenation and pH of different parts of the cancer. Poorly oxygenated tumor is less sensitive to radiation. Since large tumors frequently have poorly oxygenated area, this may be one explanation for failure of tumor control.

The goal of radiation treatment is the complete destruction of an entire tumor. In other cases, the aim is to shrink a tumor and relieve symptoms. In either case, doctors plan treatment to spare as much healthy tissue as possible.
 Radiation therapy may be used to treat almost every type of solid tumor, including cancers of the brain, breast, cervix, larynx, lung, pancreas, prostate, skin, spine, stomach, uterus, or soft tissue sarcomas. Radiation can also be used to treat leukemia and lymphoma. Radiation dose to each site depends on a number of factors, including the type of cancer and whether there are tissues and organs nearby that may be damaged by radiation.

For some types of cancer, radiation may be given to areas that do not have evidence of cancer. This is done to prevent cancer cells from growing in the area receiving the radiation. This technique is called prophylactic radiation therapy.

Radiation therapy also can be given to help reduce symptoms such as pain from cancer that has spread to the bones or other parts of the body. This is called palliative radiation therapy.

External radiation therapy usually is given on an outpatient basis; most patients do not need to stay in the hospital. External radiation therapy is used to treat most types of cancers. In addition, external radiation may be used to relieve pain or ease other problems when cancer spreads to other parts of the body from the primary site.
1.7. Treatment of cancer – physical approach

The fundamentals of cancer are the fundamentals of growth. Physics offers biology tools and techniques to attack the disease. The connection between physics and cancer is peculiar as intimate as cause and effect. Radiation in the treatment of cancer can itself cause cancer.

The first step is an examination of the contributions that physics can make to the larger problem of growth, rather than the treatment of cancer. The physicist’s role will be quite different from that of a biologist. The biologist wants techniques the physicist believe that his greatest contributions conceptual.

Since the inception of radiotherapy soon after the discovery of x rays by Roentgen in 1895, the technology of x ray production has first been aimed towards even higher photon and electron beam energies and intensities, and more recently towards computerization and intensity modulated beam delivery. During the first 50 years of radiotherapy the technological progress was relatively slow and mainly based on x ray tubes, van de graff generators and betatrons.

The invention of the Co-60 teletherapy unit by H.E.Johns in Canada in the early 1950s provided a tremendous boost in the quest for higher photon energies and placed the cobalt unit at the forefront of radiotherapy for a number of years.
The concurrently developed medical linear accelerators (linacs), soon eclipsed cobalt units, moved through five increasingly sophisticated generations and became the most widely used radiation source in modern radiotherapy. The linac offers excellent versatility for use in radiotherapy through isocentric mounting and provides either electron or megavoltage x ray therapy with a wide range range of energies.

In addition to linacs, electron and x ray radiotherapy is also carried out with other types of accelerator, such as betatrons and microtrons. More exotic particles such as protons, neutrons, heavy ions and negative π mesons, all produced by special accelerators, are also sometimes used for radiotherapy. Most contemporary radiotherapy is carried with linacs or teletherapy cobalt units.

In addition to the routine conventional radiotherapy techniques used in standard radiotherapy departments and clinics, several specialized techniques are known and used for special procedures whether it is in dose delivery or target localization.

The radiotherapy techniques that currently fall into the specialized category are as follows. The first six are special dose delivery techniques, the last three are special target localization techniques.

1) Stereotactic irradiation 2) Total body irradiation (TBI) with photon beams 3) Total skin electron irradiation (TSEI) 4) Intraoperative
radiotherapy(IORT) 5) Endorectal irradiation 6) Conformal radiotherapy and Intensity modulated radiotherapy(IMRT) 7) Image guided radiotherapy(IGRT) 8) Respiratory gated radiotherapy 9) Positron emission tomography(PET)/Computed tomography(CT) fused images.

**Stereotactic irradiation**

It is the term used to describe focal irradiation techniques that use multiple non-coplanar photon radiation beams and deliver a prescribed dose of ionizing radiation to preselected and steriotactically localized lesions, primarily in the brain. With regard to dose fractionation, this technique is divided into two categories. One is Stereotactic radiosurgery in which the total dose is delivered in a single session. The other is Stereotactic radiotherapy in which the total dose is delivered in multiple fractions like in standard radiotherapy. The diseases treated with this technique are functional disorders, vascular lesions, primary benign and malignant tumours and metastatic tumours.

**Total body irradiation (TBI)**

It is a special radiotherapeutic technique that delivers to a patient’s whole body a dose uniform to within 10% of the prescribed dose. Megavoltage photon beams, either Co-60 gamma rays or megavoltage x rays are used for this purpose.
Total skin electron irradiation (TSEI)

It is a special radiotherapeutic technique that aims to irradiate the patient’s whole skin with the prescribed radiation dose while sparing all other organs from any appreciable radiation dose. Since skin is a superficial organ, the choice of electron beams for the treatment of generalized skin malignancies is obvious.

Intraoperative radiotherapy (IORT)

It is a special radiotherapeutic technique that delivers in a single session a radiation dose of the order of 10-20 Gy to a surgically exposed internal organ, tumour or tumour bed.

Endorectal irradiation

It is a sphincter saving procedure used in the treatment of selected rectal carcinomas with superficial x rays.

Conformal radiotherapy and Intensity modulated radiotherapy (IMRT)

The basic premise of conformal radiotherapy is that, in comparison with standard dose delivery techniques, tumour control can be improved by using special techniques that allow the delivery of a higher tumour dose while maintaining an acceptable level of normal tissue complications. Conformal radiotherapy conforms or shapes the
prescription dose volume to the PTV while at the same time keeping the
dose to specified organs at risk below their tolerance dose. The conformal
radiotherapy chain is based on 3D target localization, 3D treatment
planning and 3D dose delivery techniques.

In addition to field shaping in 2D conformal radiotherapy, in which
the radiation fields are irregularly shaped but of uniform intensity, an
MLC (multileaf collimator) may also be used to achieve beam intensity
modulation for use in 3D conformal radiotherapy. The IMRT technique is
currently the most advanced form of conformal radiotherapy and holds
great promise for improving radiotherapy both through increased tumour
control probability and decreased treatment morbidity (NTCP).

**Image guided radiotherapy (IGRT)**

The accuracy of dose delivery with IMRT and tomotherapy has
been limited by uncertainty in target localization at the time of treatment.
Interfraction as well as intrafraction target movement relative to
reference landmarks coupled with set up errors and other inaccuracies
add to this uncertainty.

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

This may allow reduced treatment margins, fewer complications, dose escalation and the avoidance of geographical misses. The ideal image guided system will allow the acquisition of soft tissue images at the time of each fraction of radiotherapy.

The physicist’s contribution to the study of cancer has been modest. The present-day use of radiation therapy is an extension of the familiar use of radium and x-ray in the treatment of cancer.

In the early days long cyclotron hours were used to the bombardment of phosphorus for the treatment of a leukemia patient. The radioactive phosphorus gets concentrated in the bone marrow where white blood cells are made. Since leukemia is characterized by the over-production of white blood cells, radio phosphorus could deliver enough radiation in the right places to control this over production.

The average prolongation of life of leukemia patients is no greater with radio phosphorus than with the more conventional x-ray treatment. The use of radioactive iodine in the treatment of thyroid cancer is found promising. Since the thyroid picks up iodine, thyroid cancer can be controlled by delivering the iodine radiation directly into the thyroid itself.
This type of treatment is useful for patients who have surgical thyroid removal and who are troubled by malignant fractions of thyroid tissue at different places throughout the body. In diagnosis of cancer, radioactive isotopes have an important role.

Brachytherapy uses radiation that is placed very close to or inside the tumor. The radiation source is usually sealed in a small holder called an implant. Implants may be in the form of thin wires, plastic tubes called catheters, ribbons, capsules, or seeds. The implant is put directly into the body.

In Interstitial radiation therapy implant wires are inserted into tissue at or near the tumor site. It is used to treat tumors of the head and neck, prostate, cervix, ovary, breast, and peri anal and pelvic regions.

Breast cancers pick up more radioactive phosphorus than do surrounding normal tissue. The uptake quality of phosphorus is best used in the diagnosis and location of breast cancers that helps in the treatment of disease.

The real contribution of physics to cancer rests in the good team work of the physicist, the chemist, the biologist who can do the basic research on the dreadful disease of cancer.
1.8. Treatment of cancer – chemical approach

Chemical agents are used to destroy cancer cells in the treatment of malignancies. The bone marrow suppressive effect of nitrogen mustard was discovered in the treatment of illness in the early 1900’s. Then onwards, the search for anti cancer activity drugs was continued and the goal of treatment with chemotherapy has evolved to cancer cure.

Chemotherapy has the advantage to treat widespread or metastatic cancer, whereas surgery and radiation therapy are limited to treating cancers with limited areas.

Chemotherapy is a systemic treatment of cancer with a combination of drugs administered at an interval. This can be done intravenously or orally. Those anti neoplastic drugs kill rapidly dividing cells including cancer cells as well as certain normal cells such as cells in the blood, in the mouth, in the stomach and bowel, in the hair follicles, in the skin, etc.

Chemotherapy always causes side effects for the reason that it involves damage to the healthy tissues also. The goal of all chemotherapy drugs is to kill the cancerous cells with minimal damage to the healthy cells. To achieve this goal, some special characteristics of the cancer cells are identified that are not found on normal tissue.
A distinct cancer cell feature could serve as a potential target for a chemotherapy drug and thereby spare normal tissues. That is the cancer cells grow faster than normal cells. To target the cell growth cycle is one aspect. Fast-growing cells would be affected the most and slow-growing cells would be least disturbed.

This is the basis for many chemotherapy agents. Hair follicles, skin, and the cells that line the gastrointestinal tract are most sensitive to the effects of chemotherapy. Therefore the cancer patient experience side effects like hair loss, rashes, and diarrhea etc.,

The human body processes and excretes all drugs through either the liver or the kidneys. Therefore, when a patient has kidney or liver damage, giving chemotherapy becomes precarious. Administering the recommended amount of drug may prove to be too toxic in a patient unable to metabolize and excrete it. Kidney and liver damage limits the patient’s chemotherapy options.

The understanding of the normal cell cycle and the behavior of cancerous cells helps to understand how chemotherapy works to destroy cancer cells. The cell cycle is divided into four phases: the G 1, S, G 2, and M phases. A chemotherapy agent may work only in one phase of the cycle or be active in all phases.
G 1 phase is the most active in protein synthesis. The cellular DNA at this phase is tightly coiled and is not actively being transcribed (copied). Few chemotherapy agents are active at this phase of the cell cycle. By contrast, the S phase is the synthetic phase of the cell cycle. DNA replication is most active in this phase and many chemotherapy agents work in this phase. G 2 represents a time when mostly RNA (and some protein) is actively produced.

Mitosis, or actual cell division, occurs during the M phase. There are two major classes of chemotherapy drugs that are most active during this phase of the cell cycle. Chemotherapy drugs can be prepared keeping in view in which phase the drugs effectively kill the maximum tumour cells.

Most chemotherapy agents kill cancer cells by affecting DNA synthesis in the cell cycle. The major categories of chemotherapy agents are alkylating agents, anti metabolites, anthracyclines, and plant alkaloids, anti tumor antibiotics, taxanes, and platinums.

Alkylating agents are the oldest class of anticancer drugs. Almost all of these drugs are active or latent nitrogen mustards. Nitrogen mustards are various poisonous compounds originally developed for military use. They work by attacking the negatively charged sites on the DNA i.e., oxygen, nitrogen, phosphorous and sulfur atoms.
By binding to the DNA, the processes of replication, transcription, and base pairing leading to duplication of the cell’s genetic material are significantly altered. Alkylation of DNA leads to DNA strand breaks and DNA strand cross-linking. By altering DNA in this manner, cellular activity is stopped and the cell dies.

Plant alkaloids are a group of chemotherapy agents obtained from plant materials. They are broken down into four groups: topoisomerase inhibitors, epipodophyllotoxins, taxanes and vinca alkaloids. These drugs are used in many solid and liquid tumors. The side effects of these drugs vary from drug to drug.

Many chemotherapeutic agents affect healthy cells and organs, the patient's laboratory data should be checked before chemotherapy administration, including white blood cell count, hemoglobin/hematocrit, platelet count, renal function tests, and liver function tests. Abnormalities in any of these values may require dose adjustments or the delay of therapy. Increased intravenous fluids or administration of anti-nausea medicines are needed to decrease the side effects.

There are substantial short-and long-term side effects from chemotherapy. Short-term side effects include the toxic effects encountered during chemotherapy, while long-term side effects include later complications of treatment arising after the conclusion of adjuvant
Chemotherapy. These side effects vary, depending on the specific agents used in the adjuvant regimen as well as on the dose used and the duration of treatment.

1.9. Treatment of cancer – Surgical approach

Surgical oncology is the application of surgical principles in the speciality of oncology. These principles have been evolved by adapting certain standard surgical procedures as per the situations that arise when dealing with cancer patients.

The surgeon is a specialist who sees the patient with a solid malignancy. The surgeon will be contacted and the support of that surgical oncology speciality will be taken at the time of diagnosis, therapy, palliative and rehabilitation modalities. In each of the above areas, the guidance from surgical oncologist is inevitable.

The surgeons should assess the intra operative risk factors to attend the complications such as blood loss and hypotension. During surgeries wide resections are done even though resections with little margins are sufficient for the tumours that are sensitive to radiation and in case of planning the adjunctive radiation therapy. The other surgical procedures to estimate treatment adequacy in oncology are preventive and palliative aspects. Surgery can be decided by taking into the type of
cancer, its metastatic potential, the intended adjunctive radiotherapy and chemotherapy.

Surgery done at the first instance stands the best chance from the curative point of view. The surgery must be planned to excise the tumour mass completely. If some tumour cells are left unexcised, they should be treated with adjunctive therapy. Surgical planning has to be done based on the tumor type, its clinical stage and its biologic response.

There are four boundaries of surgical resection. They are radical, wide, marginal, and debulking. Recurrence of tumours occur, if they are not fully excised and such kind of recurrent tumours are very much invasive due to changes in the vascularity and the immune response. If the first surgery is not done properly, the subsequent ones will be more difficult due to the destruction of evenness of surgical planes suitable for operation.

Surgery is the best modality of cancer therapy and it is the choice for the treatment of solid tumors. The cancer surgeon has the responsibility to confirm the tissue diagnosis through a biopsy with an operative procedure or by an imaging modality. The cancer surgeon communicates the biopsy findings to the patient, regarding the stage of the disease and arranges communication of the patient with the other oncology team. The cancer surgeon must be aware of the history of the
malignancy, its various treatment modalities to plan for the multimodality treatment algorithm.

It is also the cancer surgeon’s responsibility to provide the first hand information about the prognosis of the disease for the follow-up care and the possibility of tumor recurrence. Therefore the cancer surgeon’s commitment towards the patient’s disease is many fold unlike any other surgical specialist, in terms of acute and long term results.

In the olden days, surgeons used to treat cancer conservatively by removing only the gross lesion. This led to extremely high rates of local recurrence and subsequent patient mortality. Due to this, surgeons opted for complete en bloc resections and amputations to treat patients with malignant lesions.

These procedures were not appreciated well even though the results were good. With the advent of complementary and effective treatment modalities such as radiation therapy and chemotherapy, the surgical resection procedures became conservative again.

In the treatment of localized primary tumours and the lymphatics around, surgery plays an active and effective role. This can be possible by en bloc surgical procedures of the gross and microscopic tumor in all vulnerable anatomic locations. Surgery does not have much role in the management of cancer when the tumour spreads from the primary site to
a distant location. But prolonged survival is possible after the surgical resection of some metastases in the lung, liver, or brain. A 5-year survival rate up to 40% can be expected after surgical resection of solitary colorectal metastasis in the liver.

In surgical procedures, 100% of excised tumour cells are killed. Whereas in either chemotherapy or radiotherapy, only a fraction of tumour cells are killed by each treatment. The tumour burden can be reduced with surgical resection of the microscopic disease while enhancing the potency of the other adjuvant therapies and reducing the risk of recurrence.

1.10. Survey of literature on pathological, biochemical, histological, radiation aspects of cancer

William J. Mayo (1920) reported that the increase, in the size of the nucleolus, as well as the nucleus, means not only rapid and uncontrolled production of cells but cells without function, which is characteristic of cancer.

Brues, et al (1951) reports key problems of molecular oncology. Malignant cell growths based on autonomic and unlimited proliferation of a cell clone expanding out of its own tissue and growing inn on-homologous tissues. All attributes of euplastic cells reflect certain peculiarities of behavior of normal cells in some conditions and so full
understanding of the nature of malignant growth is impossible without full understanding of cell biology.

Pohl (1951) observed the translational motion of neutral matter caused by polarization effect in a non uniform electric field and named it as dielectrophoresis. Till then the study of NUFE on neutral matter was not recognized as a separate phenomenon.

Antipenko (1963) found lymphosarcoma in one of the dogs alive 27.5 months following exposure to 6.5 Gy of radiation with subsequent symptomatic treatment. 8 months after the exposure the dog was no different from the others in the group.

Solomonreidar Sognnaes (1965) observed that, the fundamentals of cancer are the fundamentals of growth. Physics offers biology tools and techniques to attack the disease, but both sciences must work together on the basic problems of growth. The connection between physics and cancer is peculiar as intimate as cause and effect. For radiation, a valuable agent in the treatment of cancer can itself cause cancer.

This curious interrelationship exists largely because no one knows what causes growth, whether it be normal or abnormal. The primary problem in cancer is not an exploration of such isolated problems as the connection between radiation and cancer. It is the much larger and
much more stimulating problem of understanding the fundamentals of growth.

Alekseyev (1970) reported data on spontaneous remissions in 104 people with acute leukemia of which in 67 the cause of remissions were festers in 35 infections and in 2 pneumonia. Some infected caused remissions were as long as 10 years and fester caused are 12 years.

Kassirsky, et al (1970) reported hopeless cases of chronic lympho leukemia in which both clinical and hematological signs of the disease disappeared. Their remissions and cures seem to be attributable to the activation of the organism’s protective mechanisms notably due to the immunological protection.

Singar, et al (1972) considered the living cells comprising of salty polar interior fluid material surrounded by a membrane or a wall and stated that this membrane has a lipid layer bounded on both sides by a polar surface that produced bound and diffused couturier layers having a high polarisability of a cell in low to moderate frequencies of AC fields.

Petrini, et al (1977) investigated that both T and non-T lymphocytes decreased immediately following radiotherapy in breast cancer patients. There was no difference in the proportion of T and non-T lymphocytes between patients with and without metastases, respectively.
Crane, et al (1978) used the balance cell technique to determine excess permittivity of different individual yeast cells under various conditions and compared with those predicted from those of the theoretical model of yeast cells.

Pohl (1980) investigated that the cells in the reproductive state seem to act like signal generators emitting radiation which are detectable by small polarisable particles nearby in a suitable medium and also reported micro dielectrophoretic technique. Cells in the reproductive state such as murine sarcoma cells and rapidly growing murine fibroblasts were found to attract highly polarisable small particles.

Kavetsky (1981) reported that tumors were favored immune depressive state attributable to numerous factors such as hereditary, age, post infection depressed reactivity.

Mazurenko (1982) reported the virus etiology of numerous malignant tumors in animals except burkitts lymphoma which is to be found in some African areas on rare occasions. Human cancer is not a contagious disease. Its basic causes are the processes inside the organism which are triggered by the aging or misbalance of its systems in a younger age.

Gopala Krishna, et al (1983) reported the dielectrophoretic collection rate (DCR) of yeast cells considering cylindrical field geometry.
The excess permittivity of individual yeast cells was determined by subjecting them to both dynamic and static single cell dielectrophoresis.

Harry V. Gelbo (1983) presented a report on biochemistry of cancer. The subjects of the section meetings were Metabolism and Enzymes, Proteins, Nucleic Acids, and the Biochemistry of Carcin.

A survey by IAEA, Vienna (1997) reported that the major application of blood and blood component irradiation is for the prevention of graft-versus-host disease in immune deficient patients by the abrogation of T-lymphocytes.

However, a potential application of this technology would be for the sterilization and inactivation of pathogenic microbes in contaminated blood products. The purpose of this report is to review relevant literature on the effect of ionizing radiation (essentially gamma and X-rays) on whole blood, blood cells and other blood components in order that a rational decision can be made on the feasibility of their irradiation whether for sterilization (or decontamination), or alternatively, for inactivation of a particular blood component

Santa Maria, et al (1985) studied dielectrophoretic collection of the suspensions of macromolecules such as polyvinyl chloride and sephadex G-50 as a function of applied electric field and concentration.
Dmitrov and zhelev (1987) studied dynamic cell dielectrophoretic mobilities of chloroplasts, erythrocytes; lymphocytes etc in the frequency range 1KHz to 12MHz at different medium conductivities and ion concentrations.

Gopala Krishna, et al (1988) studied the behavior of erythrocytes belonging to animals of different locomotion using the dielectrophoretic spectroscopy by subjecting them to spherical field geometry.

Gopala Krishna, et al (1989) studied the dielectrophoretic collection rate of human, frog, chicken and pigeon erythrocytes using spherical field geometry. The differences in DCR spectra were attributed to the variations in the electric make up of the cell and also they studied the influence of physical variables such as the frequency, voltage of the applied electric field suspension conductivity cell concentrations and exposure time of the cell to the non uniform electric field on DCR spectra of human erythrocytes using cylindrical field geometry in the frequency range of 3 KHz to 1.5 MHz. Their results were in the conformity with the theory of dielectrophoresis.

Akoev (1989) reported on the research in virus origins of leukosis and cancer notably with mice and chickens and investigated the possible virus origin of tumor and leukosis in man and obtained the whole set of
epidemiological, clinical, pathophysiological, cytological, and biochemical evidence.

Gareth (1989) reported that most cancers arise from one mutation in a single cell and so represent monoclonal proliferation, although further mutations are enviable as the tumor grows. There are approximately $10^9$ cells within one cubic centimeter of tissue and most cancers are substantially larger than this when first detected.

Williams Chris (1990) reported many cancers accumulate chromosomal abnormalities. For years it was unclear whether these were etiologically important or whether there was just a consequence of chaotic growth. Certain abnormalities were found to have a high degree of specificity for particular cancer such as Philadelphia chromosome found in chronic myeloid leukemia in 1960.

Gopala Krishna, et al (1991) reported the dielectrophoretic collection rate of erythrocytes of A, B, AB, O blood groups as a function of frequency was determined using spherical field geometry for different tonacities. Their results indicate significant variation in the hypotonic and hyper tonic conditions compared to isotonic behavior.

Marszalek, et al (1991) have described a novel design for measuring the complete dielectrophoretic spectrum of a single cell. From the analysis of the dielectrophoretic spectrum, the membrane
conductivity, sigma membr, and the membrane dielectric permittivity, epsilon membr, of the cell may be determined according to the theory of dielectrophoresis. The values for the slime cells were compared with values obtained by the dielectric spectroscopy method which measures average values for cells in suspension.

Charles W. Boone, et al (1992) studied Intraepithelial neoplasia is of critical importance to the cancer chemoprevention field because it is a target condition for which drugs must be sought that will prevent its development or stop its progression.

Gopala Krishna, et al (1994) reported the influence of thrombosis on dielectrophoretic collection of human erythrocytes. Dielectrophoretic collection rate of normal and diseased human erythrocytes were studied by varying the frequency of applied field from 1 MHZ to 10 MHZ. keeping all other parameters to be constant and measured the characteristic frequencies from DCR spectra.

Gopala Krishna, et al (1995) studied human red blood cells of normal and cancer blood by using principle of dielectrophoresis. The threshold voltage for the dielectrophoretic collection of normal and diseased HRBC collected from healthy persons and patient suffering from leukemia were reported in the β –dispersion region under the action of non uniform electric field set by spherical field geometry. Significant
variation was observed in the threshold voltage for collection of normal and cancer samples at the same frequencies under identical conditions of the experimentation.

Sheard, et al (1999) reported the findings about the palliative care of two meta-analyses of trials of psychological interventions in patients with cancer are presented: the first using anxiety and the second depression, as a main outcome measure. The majority of the trials were preventative, selecting subjects on the basis of a cancer diagnosis rather than on psychological criteria. The findings suggest that preventative psychological interventions in cancer patients may have a moderate clinical effect upon anxiety but not depression. There are indications that interventions targeted at those at risk of or suffering significant psychological distress have strong clinical effects.

Narayanan (2000) reported that biological effects of radiation results from radiation induced chemical biochemical changes. Radiation can cause genetic mutations and cell damage. Charged particles such as x rays and γ rays and neutrons damage indirectly where as α rays and electrons damage biological tissues directly.

Robert (2001) studied the surgical pathology had its beginnings in the late 1800s. This paper touches on a few representative aspects in the history of Head and Neck Pathology during the past 130 years.
Published online reports of *British Journal of Cancer* (2002) reveals that Hepatocellular carcinoma (HCC) ranks among the most common malignancies in China, Japan, Southeast Asia, South Africa and some South European areas. Early detection of metastatic tumour cells is critical to identify HCC patients at high risk of relapse and for the prescriptive therapy. However, it is difficult to detect such dissemination of HCC cells through blood route with conventional techniques.

Constantine G Loukas, et al (2003) reported that, Image analysis is a rapidly evolving field with growing applications in science and engineering. In cancer research, it has played a key role in advancing techniques of major diagnostic importance, minimising human intervention and providing vital clinical information.

William R Ware (2003) observed in his *Low-Dose Radiation Exposure and Risk of Cancer*, modern medicine makes ever increasing use of imaging with x-rays and radiation from infused radioactive isotopes, both for primary diagnosis, whole-body CT screening and for guiding invasive procedures such as angiograms, stent placement, etc.

therapy has become a standard treatment option for a wide range of malignancies.


Julius M. Lipta (2007) observed that Surgery, to treat cancer, is one of the most common procedures performed in small animal practice. Clinicians should identify potential intraoperative risk factors, such as blood loss and hypotension, and be prepared to address these complications. Depending on the tumor type and metastatic potential and the completeness of excision, adjunctive radiation therapy and chemotherapy should also be considered.

Julia Draznin (2007) presented the goal of all chemotherapy drugs is to kill the cancerous cells, while using a dose that causes the least harm the body’s healthy cells. A distinct cancer cell trait could serve as a potential target for a chemotherapy drug and thereby spare normal tissues. One feature that is seen in most cancer cells is that they grow at a rate faster than normal cells. Therefore, targeting some aspect of the
cell growth cycle seems reasonable. Fast-growing cells would be affected the most and slow-growing cells would be least disturbed. In fact, that is the basis for many chemotherapy agents. This is apparent when considering the side effect profiles of most chemotherapy drugs.

DeVita, Jr, et al (2007) states improvement of diagnostic markers for detection of malignant potential and clinically silent metastasis formation as well as design of more effective therapies to treat metastatic diseases.


A study based on computer modeling of radiation risk suggests that widespread screening for the buildup of calcium in the arteries using computed tomography scans would lead to an estimated 42 additional radiation-induced cancer cases per 100,000 men and 62 cases per 100,000 women, according to a new report (Science Daily, 2009).
Remy Vixamar (2009) studied the Side effects of chemotherapy and radiation, Reported that the Formation of cancer cells results from mutation of normal cells that escape the normal restraint on cell division. That is, those cells function differently of other cells in a tissue. This anomie causes the development of cancer cells, which gradually multiply and possibly affect other normal tissues (metastasis). Without medical intervention, this abnormal overgrowth can cause a general degeneration of your body, and sometimes death. To stop the abnormal proliferation, your oncologist can use chemotherapy, radiation or both.

Lawrence D. Wagman, (2009) reported that Surgical oncology, as its name suggests, is the specific application of surgical principles to the oncologic setting. These principles have been derived by adapting standard surgical approaches to the unique situations that arise when treating cancer patients.

Raphael E. Pollock, et al (2009) observed that, Surgery is the oldest modality of cancer therapy and still forms the mainstay of treatment in solid tumors. The cancer surgeon is commonly charged with the responsibility to establish a tissue diagnosis for a suspicious lesion, where it will be the surgeon’s decision whether an operative procedure is needed versus an image-directed or other biopsy approach.
Stephen Strum (2009) reported that Patients with malignant disorders and/or internal medicine problems can greatly benefit from integrative care — a combination of Eastern, Western and non-conventional approaches that often involve so-called alternative therapies.

A study in 2009 reported that Oncology is undoubtedly the most rapidly growing subspecialty in the field of medicine, and breast cancer is one of the most serious problems of oncology. It is the leading cause of death of women in many countries and is truly a multidisciplinary problem without geographic restrictions (Journal no. 10549 Springer (2009))

Stuklov (2009) made a study and enrolled 177 women with gynecological cancer and 132 with gynecological disease. Hemoglobin (Hb), mean corpuscular hemoglobin (MCH), red blood cells (RBC), and erythrocyte sedimentation rate (ESR) were analyzed. The gynecological patients with anemia showed a correlation between Hb and MCH (\(p < 0.05\)), which is indicative of iron deficiency.

In the gynecological cancer patients, the correlation between Hb and MCH was significant (\(p < 0.01\)), that between Hb and RBC was strong (\(p < 0.001\)), suggesting the reductions in both erythropoiesis and Hb synthesis in the erythrocytes. In these patients, anemia results
from chronic diseases. The gynecological cancer patients were found to have higher ESR and lower Hb, RBC, and MCH than the gynecological patients.

1.11. Genesis of present investigation

A survey of literature reveals that a large number of investigations have been carried out to explain the principles of radiation oncology, radiation dose exposure, cancer principles and practice of radiation oncology, radiation and chemotherapy side effects, effects of ionizing radiation on blood and its components under different experimental conditions by adopting different methods.

Blood and plasma are the fluid connective tissues of the biological organism such as human beings. Any disease such as cancer spreads in the body using blood as the medium of transport. The effect of radiation can be noticed by studying the different clinical parameters of the blood such as Hemoglobin (Hb), RBC, WBC, Platelets, ESR, size of erythrocytes, viscosity, volume flow rate and surface tension of blood and plasma, pH, electrical conductivity, refractive index and dielectrophoresis of blood and plasma.

Even though quite an extensive literature is available on human red blood cells of persons enjoying normal health studied under different
techniques, information on clinical parameters of cancer blood, biophysical parameters of cancer blood and the comparative study between normal persons and cancer patients regarding the above two factors is scanty.

The present investigation has therefore been attempted to study the clinical and biophysical parameters such as Hb content, RBC, WBC, Platelets, ESR of erythrocytes, size of erythrocytes of blood, pH of blood and plasma, viscosity, surface tension, volume flow rate of blood and plasma, electrical conductivity, refractive index, dielectrophoresis of blood and plasma of normal persons and cancer patients. It can be mentioned here that the above parameters are studied by taking a cross section of around 100 patients suffering from different types of cancers at different stages.

The present study is an attempt to find out the effect of radiation treatment on the blood and other parameters of cancer patients. It is in this context the author made an attempt to find out any change in the composition of blood of the cancer patients by conducting various biophysical investigations.