

**RADIATION THERAPY COMBINATION OF CISPLATIN INVOLVED IN THE
TREATMENT OF CONTRASTING CANCER EPITOME: A REVIEW**

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ABSTRACT

Cancer is a term used to describe a large group of diseases that are characterized by a cellular malfunction. Healthy cells are programmed to know what to do and when to do it and cancerous cells do not have this programming and therefore grow and replicate out of control, they also serve no physiological function and these cells are now termed as “Neoplasm”. Medically termed as “Malignant neoplasm”. Cancer is collection of disease characterized by abnormal and uncontrollable growth. The destruction of Cancer cells can result from uncontrolled cell growth and loss of cell affinity to undergo apoptosis. There are numerous numbers of cancers which can be caused to any type of cell in the organs of the body. Cancer diagnosis can be done with biopsy, endoscopy, blood test, bone marrow aspiration and genetic analysis. Treatment for cancer involves surgery, chemotherapy, Radiation therapy, targeted therapy and immunotherapy. Radiation therapy can be used in combination of cisplatin. Cisplatin is one of the most effective anticancer agents widely used in the treatment of solid tumors and generally considered as cytotoxic drugs which kills cancer cells by damaging DNA and inhibiting DNA synthesis. Combination of cisplatin and Radiation therapy in squamous cell carcinoma has highest success rate.

KEYWORDS: Cancer, radiation, contrasting cancer, clinical manifestations, myeloma, myeloid leukemia, astrocytoma, Kaposi sarcoma, chemotherapy, Radiation therapy, brachytherapy, external radiation.

INTRODUCTION

Cancer is a term used to describe a large group of diseases that are characterized by a cellular malfunction.^[1] Cancer cells develop because of damage to DNA which direct all activities in each cell. When DNA becomes damaged the body is usually able to repair it. In Cancer cells however the damaged DNA is not repaired people can inherit damaged DNA which results in approximately 10% of all cancers more often when a person's DNA becomes damaged by exposure to something in environment or random cellular events.^[2] Cisplatin is one of the most effective anticancer agents widely used in the treatment of solid tumors. Cisplatin induced DNA damage act to its various signaling

Pathways to prevent or promote the cell death. Combination of radiation and chemotherapy drugs have been shown high success rate in head and neck cancers.^[3] Concurrent chemo radiation therapy with cisplatin standard for patients with loco regionally advances squamous cell carcinoma of the head and neck and for patients with resected SSCHN with high-risk features.^[4,5]

Cancer definition – A disease caused by an uncontrolled division of abnormal cells in the part of the body. A malignant growth or tumor resulting from an uncontrolled division of cells or an evil or a destructive practice or phenomenon that it is hard to contain or eradicate.

Differences between normal cell and cancer cell.

Normal cell	Cancer cell
Small, uniformly shaped nuclei relatively large cytoplasmic volume	Large, variable shaped nuclei relatively small cytoplasmic volume
Conformity in cell size and shape cells arranged into discrete tissues	variation in cell size and shape disorganized
May possess differentiated cell structures Normal presentation of cell surface markers.	Loss of normal specialized features Elevated expression of certain cell markers
Lower levels of dividing cells Cell tissues clearly demarcated.	Large number of dividing cells Poorly defined tumor boundaries.

Development of Cancer cell – There are three phases in development of cancer cells.

- **Initiation** – A single cell undergoes a mutation that causes it to divide repeatedly.
- **Promotion** – A tumor develops and cells increase within the tumor mutate.
- **Progression** – A cell mutates in such a way that allows it to invade surrounding tissue.

Tissue changes that are not cancer - not every chain in a body is tissue is cancer some tissues may develop into cancer if they are not treated.^[1]

1. **Hyperplasia** - The enlargement of an organ or tissue caused by an increase in the reproduction rate of cells and often as an initial stage in the development of cancer.
2. **Dysplasia** - **Dysplasia** means disordered cellular development often accompanied with metaplasia and hyperplasia.
3. **Carcinoma in situ** – Carcinoma in situ represents noninvasive cancer Defined by confinement of malignant cells within basement membrane. Example lobular carcinoma in situ.

Tumor grade - Tumor grade is the description of a tumor based on how normal the tumor cells and the tumor tissue look under a microscope. It is an indicator of how quickly tumor is likely to grow and spread. If the cells of the tumor and organization of the tumor tissue are close to those of normal cells and tissues that tumor is called well differentiated. This tumor stands to grow and spread as a slower rate than tumor that are undifferentiated or poorly differentiated which have abnormal looking cells and may lack normal tissue structure.

G0- grade cannot be acid or undetermined grade.

G1- well differentiated or low grade

G2- moderately differentiated or intermediate grade

G3- poorly differentiated or high grade

G4 - undifferentiated or high grade.^[1]

Stage of cancer - tumor grade is not the same as the stage of cancer. Cancer stage refers to the size or extent of the original tumor and whether or not cancer cells are spread in the body. Cancer stage is based on factors such as location of the primary tumor, tumor size, regional lymph node involvement and the number of tumors present.^[1]

Stage	Meaning
Stage zero	Abnormal cells are present but have not spread to nearby tissue also called carcinoma in situ.
Stage 1,2,3	Cancer is present the higher the number the larger the cancer tumor and the more it has spread to the nearby tissues
Stage 4	The cancer has spread to the distant Parts of the body

Another Staging system^[1]

1. In situ - abnormal cells are present but have not spread to the nearby tissue
2. Localized - cancer is limited to the place where it started with no sign that it has spread
3. Regional - cancer has spread to the nearby lymph nodes, tissues or organs
4. Distant - cancer has spread to the distant Parts of the body
5. Unknown - there is not enough information to figure out the stage.

Epidemiology

- Data according to NCRP 2020 - cancer in India rise from 13.9 lakh to 15.7 Lakh in the year 2020 by 2025. The total number of cases in males are estimated to be 67941 in 2020 which may rise 76375 in 2025. In females are estimated to be 712578 in 2020 and 806218 in 2025.^[6]
- Andhra Pradesh state occupies 9th place of having higher cancerous patients in India.
- The most common forms of Cancer found in India are breast cancer, cervical cancer and oral cancer. Typically found among women of age 40 and above.
- In Andhra Pradesh breast cancer occupies the top position followed by lung cancer and cervical cancer.

Etiology^[7]

- Chronic inflammation, obesity, oxidative stress, pharmaceutical drugs, toxicity, acidity, environmental toxins, smoking, alcohol, stress insomnia, genetics, type 2 diabetes, sedentary Lifestyle, weakened immunity, poor diet, nutritional deficiencies (micronutrient deficiencies, vitamin deficiency, mineral deficiencies, other deficiencies).
- Conversion of proto-oncogenes (potential for cell transformation) to oncogenes (cell transformation)
- Alteration in tumor suppressor genes.^[8]

Spread of cancer: cancer that has spread from the place where it first formed to another place in the body is called metastatic cancer. Metastatic cancer has the same name and same type of cancer cells as the original for primary cancer. For example, breast cancer that forms a metastatic tumor in the lung is metastatic breast cancer but not lung cancer.^[1]

A to Z cancer types^[1]

1. **Acute lymphoblastic leukemia** - type of cancer in which bone marrow makes too many Lymphocytes and leukemia may affect red blood cells, white blood cells and platelets. Symptoms may include enlarged lymph nodes, bruising, fever, bone pain and bleeding from the gums and frequent infections.

2. **Acute myeloid leukemia** - it progresses rapidly with myeloid cells interfering with the production of normal white blood cells, red blood cells and platelets, symptoms include fever, recurrent infections and bruising of the body easily.
3. **Adrenocortical carcinoma** - adrenocortical carcinoma is a rare disease in which malignant cancer cells form in the outer layer of the adrenal gland. Having certain genetic conditions increase the risk of adrenocortical carcinoma. Symptoms of adrenocortical carcinoma include pain in the abdomen.
4. **Kaposi's sarcoma** - Kaposi sarcoma is a type of cancer that can form masses in the skin, in lymph nodes and in the mouth and in other organs. Skin lesions are usually painless, purple and may be flat or raised.
5. **Aids-related lymphoma** - it is a disease in which malignant cells form in lymph systems of the patients who have acquired immunodeficiency syndrome. There are many different types of lymphoma. Symptoms may include weight loss, fever and drenching night sweats.
6. **Primary central nervous system lymphoma** - primary central nervous system lymphoma is a disease in which malignant cells formed in lymph tissue of brain or spinal cord. Symptoms include nausea and vomiting seizures, headaches and leg weakness, confusion, double vision, hearing loss.
7. **Anal cancer** - anal cancer is a disease in which malignant cells form in the tissue of the anus. Most anal cancer related to human papillomavirus infection. Symptoms of Anal cancer include bleeding from anus and rectum or a lump near the anus.
8. **Astrocytoma** - astrocytoma is a type of cancer that can form in the brain or spinal cord astrocytoma begins in the cells called astrocytes that support Nerve cells. Astrocytoma symptoms depend on the location of your tumor. Astrocytoma that occurs in the brain can causes headache and nausea. Astrocytoma that occurs in spinal cord can cause weakness and disability in the area affected by the growing tumor.
9. **Basal cell carcinoma of the skin** - basal cells produce new skin cells as old ones die. limiting Sun exposure can help prevent the cells from becoming cancerous. Disconcert typically appears as a white waxy lump or a brown scaly patch on son exposed areas such as face and neck.
10. **Bile duct cancer** - bile duct cancer is a rare disease in which malignant cells form in the bile ducts. A network of tubes called ducts connect the liver, gallbladder and small intestine. Symptoms include yellow skin and Eyes. Intensively itchy skin and stool that's white in color.
11. **Bladder cancer** - bladder cancer is a common type of cancer that begins in the cells of the bladder. Bladder cancer typically affects the older adults. It's usually diagnosed early. It's likely to recover so follow-up tests are typically recommended the most common symptoms is blood in the urine.
12. **Bone cancer (includes Ewing sarcoma and osteosarcoma and malignant fibrous histiocytoma)**- A mass of unusual cells growing in bone. Most bone tumors are and cancerous. Causes of bone tumors include abnormal healing of injury or inherited conditions and Radiation therapy. A bone tumor may cause a painless mass. Some people have dull, aching pain.
13. **Breast cancer** - breast cancer is a type of cancer that starts in the breast. Cancer starts when cells begin to grow out of control. Symptoms of breast cancer include a lump in breast, bloody discharge from nipple and changes in the shape or texture of the nipple or the breast.
14. **Bronchial tumors** - eye cancer that begins in the lungs and most often occurs in people who smoke. Two major types of lung cancer are non-small cell lung cancer and small cell lung cancer. Symptoms include cough, chest pain, wheezing and weight loss.
15. **Burkitt lymphoma or non-Hodgkin lymphoma** - an aggressive type of B cell non-Hodgkin lymphoma that occurs most often in children and young adults. The disease may affect the jaw, central nervous system, bowel, Kidneys, ovaries or other organs.
16. **Carcinoid tumors** - a slow growing cancer tumor that can grow in several places throughout the body. Carcinoid tumor often begins in stomach, appendix, small intestine, colon, rectum and lungs. Symptoms include diarrhea and skin flushing.
17. **Cardiac tumor** - A cardiac tumor is an abnormal growth of tissue in the heart and may be classified as either cancerous or non-cancerous. Further classified as primary (Originating within the heart itself) or secondary (spread from primary tumor in a different part of the body). Symptoms may include heart failure, heart murmur, palpitations, shortness of breath, chest pain, tightness of chest.
18. **Medulloblastoma** - Medulloblastoma is the most common type of cancerous Brain Tumor in children. Brain Tumor starts in the lower back part of the brain(cerebellum). Symptoms are balance problems are clumsiness, dizziness, changes in thinking ability, tiredness and lack of energy, headache, hearing loss.
19. **Germ cell tumor** - germ cell tumors are growth of the cells that form from reproductive cells. The tumors may be cancerous or not cancerous. Most germ cell tumors occur in the testicle or the ovaries. Symptoms are constipation or trouble holding pee if the tumor is in the pelvis, Leg weakness if the tumor presses on the Nerve as the bottom of the spine, a testicle of an unusual shape or size.
20. **Cervical cancer** - cervical cancer is a type of cancer that occurs in the cells of the cervix the lower part of the uterus and connects to the vagina.^[9] Symptoms include bleeding in between periods and after sexual intercourse. Foul smelling white discharge and lower back pain or lower abdominal pain may also occur.^[10]

21. **Chordoma** - These are the tumors that can occur anywhere within the spine or the base of the skull. The two most common locations are the lower back (sacral area approximately one-third to one-half of the chordomas) and the base of the skull (approximately one third of chordomas). Symptoms are headache, visual problems, nerve or muscle weakness in the back for arms or legs, nosebleeds, running nose, bowel or bladder problems.
22. **Colorectal cancer** - colorectal cancer are also called bowel cancer, colon cancer or rectal cancer, any cancer that affects the colon and rectum. Symptoms include changes in the bowel habits, changes in stool consistency, blood in the stool and abdominal discomfort.
23. **Craniopharyngioma** - it is a rare type of brain tumor derived from pituitary gland embryonic tissue that occurs most commonly in children. But also affects adults. Symptoms include balance problems, confusion, mood swings or behavior changes, headache, increased thirst and urination, slow growth in children.
24. **Cutaneous T cell lymphoma** - it is a rare type of cancer that begins in the white blood cells and T cells. Symptoms are round patches of skin that may be raised or scaly and might be itchy.
25. **Embryonal tumor** - embryonal tumor of the central nervous system are cancerous tumors that start in fetal cells of the brain. It occurs at any age but most often occur in babies and young children.
26. **Endometrial cancer** - endometrial cancer is a type of cancer that begins in the uterus. Symptoms include pelvic pain and pain during sex.
27. **Ependymoma** - a type of Brain Tumor that begins in the cells lining in the spinal cord Central canal (fluid filled space down the center) or the ventricles (fluid filled spaces of the brain). Symptoms include headache, nausea and vomiting, pain that wakes you up, dizziness and balance problems, blurry vision or double vision, trouble with balance or walking.
28. **Esophageal cancer** - Cancer of the tube that runs from the throat to the stomach. Symptoms include trouble swallowing, unintentional weight loss, chest pain, heartburn and coughing or hoarseness.
29. **Esthesioneuroblastoma (head and neck cancer)** - a group of cancers of mouth, sinuses, nose or throat. Smoking is a significant risk factor. Symptoms are sore or lump that doesn't Heal, a persistent sore throat, trouble swallowing and changes in the voice.
30. **Retinoblastoma** - retinoblastoma is an eye cancer that begins in the retina, most commonly in children. Symptoms include vision problems, Eye Pain, redness of the white part of the eye, bleeding in the front part of eye, bulging of eye, a pupil that doesn't get smaller when exposed to bright light, a different color in each Iris.
31. **Intraocular Melanoma**- intraocular Melanoma is a disease in which malignant cells form in the tissue of the eye. Signs of intraocular Melanoma include Blurred vision or a dark spot on the Iris.^[11]
32. **Fallopian tube cancer:** primary fallopian tube cancer is rare and difficult to cure disease. It is often grouped under the epithelial ovarian cancer umbrella, together with primary ovarian and peritoneal carcinoma. Symptoms include watery or blood-stained vaginal discharge, swelling of the lower abdomen that is not associated with weight gain, A lump in the lower abdomen, pain in the lower abdomen, a sensation of pressure against the bowel or bladder.
33. **Gall bladder cancer:** cancer that develops in the gall bladder, a small organ below the liver. There may be no symptoms. If symptoms occur, they may include abdominal pain, bloating and fever.
34. **Gastric cancer (stomach cancer):** cancer that occurs in the stomach. Risk factors may include smoking and a diet of highly processed or salty foods. There may be no symptoms of stomach cancer early on. Later symptoms include feeling bloated after eating, feeling full after eating small amounts of the food, nausea, heart burn or indigestion.
35. **Gastrointestinal stromal tumor (GIST):** it is a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine. This type of tumor is thought to grow from specialized cells found in the gastrointestinal tract called interstitial cells of Cajal (ICCs). Symptoms include blood in the stool or vomit, pain in the abdomen which may be severe, feeling very tired, trouble or pain when swallowing, feeling full after only a little food is eaten.
36. **Hairy cell leukemia** - hairy cell leukemia is one of the rarest types of leukemia which is cancer of the white blood cells. It gets its name from the fine, hair like strands around the outside of the cancerous cell which is visible under a microscope. Symptoms include weakness or feeling tired, fever or frequent infections, easy bruising or bleeding, shortness of breath, weight loss for no known reason, pain or a feeling of fullness below the ribs.
37. **Hepatocellular cancer:** liver cancer begins in the cells of the liver. The most common form of the liver cancer begins in the cells called hepatocytes and is called as hepatocellular carcinoma. Symptoms include pain in the upper right part of the stomach and feeling of heaviness in your upper stomach, bloating or swelling in the stomach, loss of appetite and feelings of fullness, weight loss, weakness or deep fatigue, nausea and vomiting, yellow skin and Eyes.
38. **Histiocytosis Langerhans cell:** Langerhans cell histiocytosis is a rare disorder that can damage tissue or cause infections to form in one or more place in the body. Symptoms include swelling in abdomen causes a buildup of extra fluid, trouble breathing, yellowing of the skin and whites of eyes, itching, easy bruising or bleeding, feeling very tired, diarrhea, bloody stools.

39. **Hodgkin lymphoma** - cancer of the part of the immune system called lymphatic system. Symptoms include fatigue, fever and chills.
40. **Hypopharyngeal cancer:** it is a disease in which malignant cells form in the tissues of the hypopharynx. Symptoms include voice changes, persistent sore throat, pain or difficulty in swallowing, weight loss.
41. **Pancreatic islet cell tumor:** these are rare type of hormone producing tumors that form in tissues of the pancreas. Produces too much insulin and causes seizures, fainting and low blood sugar.
42. **Kidney cancer:** Kidney cancer is a disease that starts in the Kidneys and it happens when healthy cells in one or both Kidneys grow out of control and form a lump. Symptoms include blood in urine, pain in your back, loss of appetite.
43. **Laryngeal cancer:** laryngeal cancer is a disease in which malignant cells form in the tissues of the larynx. Use of tobacco products and drinking too much alcohol can affect the risk of the laryngeal cancer. Symptoms include sore throat and ear pain.
44. **Lip and oral cavity cancer:** cancer that develops in any part of the mouth. Risk factors include tobacco use and heavy alcohol use and human papillomavirus infection. Symptoms include a sore throat that doesn't heal and a lump or a white or red Patch on the skin inside the mouth.
45. **Merkel cell carcinoma** - is type of cancer that forms on or just beneath the skin, usually in Parts of the body that have been exposed to the sun. It is most common in older people and in people with weak and immune system. Symptoms are red or pink spots, quickly growing spot on your skin that sometimes bleeds, cysts, any fast-growing spot-on mass.
46. **Mesothelioma:** tumor of the tissue that lines the lungs, stomach and heart and other organs. Symptoms include cough, chest pain, shortness of breath.
47. **Mouth cancer:** cancer that develops in the any part of the mouth. Symptoms include a sore throat, white or red Patch on inside of the mouth.
48. **Mycosis Fungoides:** diseases in which Lymphocytes become malignant and effect the skin. Symptoms include red rash on the skin.
49. **Nasal cavity and paranasal sinus cancer:** cancer that forms in the tissues of the paranasal sinuses (small hollow spaces in the bones around the nose) or nasal cavity (the inside of the nose). Most common type of nasal sinuses and nasal cavities cancer are squamous cell carcinoma. Symptoms include nasal condition and stuffiness that doesn't get better or even worsens.
50. **Neuroblastoma:** neuroblastoma is a type of cancer that forms in certain types of nervous tissue. Often found in the small glands on top of the Kidneys. Symptoms include loss of appetite and fever.
51. **Osteosarcoma:** osteosarcoma is a type of bone cancer that begins in the cell that forms bones. Symptoms include localized bone pain and swelling.
52. **Ovarian cancer:** cancer that begins in the female organs that produce eggs. Symptoms include loss of appetite and weight loss.^[12]
53. **Paraganglioma:** it is a rare neuroendocrine neoplasm that may develop at various body sites. Symptoms include high blood pressure, headache, heavy sweating for no reason, being shaky, being extremely pale.
54. **Parathyroid cancer:** parathyroid cancer is rare disease in which malignant cells form in the tissues of parathyroid gland. Symptoms include weakness and lump in the neck.
55. **Pheochromocytoma:** it is a rare usually non-cancerous tumor that develops in an adrenal gland. Symptoms include high blood pressure, Rapid Heartbeat and headache.
56. **Pituitary tumor:** pituitary tumor is an abnormal growth in the pituitary gland. Symptoms include vision changes and headaches. Hormones can also be affected interfering with menstrual cycles and causing sexual dysfunction.
57. **Pleuro pulmonary blastoma:** it is rare fast-growing cancer that forms in the tissues of the lung and the pleura. Symptoms include cough, trouble breathing, fever, lung infections such as pneumonia, pain in the chest or abdomen.
58. **Prostate cancer:** cancer in a man's prostate, a small wallet size at gland produces seminal fluid. Symptoms include difficulty with urination and sometimes there are no symptoms at all.
59. **Rectal cancer:** cancer of the colon and rectum located in the digestive tracts lower end. Symptoms include changes in stool consistency and blood in the stool and abdominal discomfort.
60. **Rhabdomyosarcoma:** it is a type of cancer of soft tissue and connective tissue or bone. Symptoms include a persistent lump or swelling in a part of the body, bulging of the eyelid, headache and nausea, trouble in urinating, bleeding from the nose, throat, vagina or rectum.
61. **Salivary gland cancer:** the cancer in which malignant cells form in the tissues of the salivary glands. Symptoms include a lump in the area of the ear, cheek, jaw. Fluid draining from the ear, trouble swallowing or opening of the mouth widely, numbness or weakness in the face.
62. **Thymoma and thymic carcinoma:** thymoma and thymic carcinoma diseases in which malignant cells form on the outside of the surface of the thymus. Signs and symptoms of thymoma and thymic carcinoma include cough and chest pain.
63. **Thyroid cancer:** cancer of the thyroid the butterfly shaped gland on at the base of the neck. Symptoms include a lump in the neck.
64. **Uterine sarcoma:** uterine sarcoma is a disease in which malignant cells form in the muscles of the

uterus or other tissues that support the uterus. Symptoms include unusual bleeding from the vagina.

65. **Vaginal cancer:** is a form of anal cancer that makes up about 4% of the cases. This type of cancer begins within the walls of the vagina not on the surface. Symptoms include vaginal bleeding.
66. **Vulva cancer:** a type of cancer that occur on the outer surface area of female genitals. Symptoms include itching.
67. **Wilms tumor:** type of childhood cancer that starts in the Kidneys. Symptoms include stomach pain, swelling of stomach, fever, nausea, lack of appetite, blood in the urine.

Types of cancer treatment^[13]

- **Biomarker testing for cancer treatment:** biomarker testing is a way to look for genes, proteins and other substances that can provide information about cancer. Biomarker testing can help to choose a cancer treatment.
- **Chemotherapy:** chemotherapy is a type of cancer treatment that uses drugs to kill cancer cells and also used to shrink tumors that are causing pain and other problems.
- **Hormone therapy:** hormone therapy is a treatment that slows or stops the growth of breast and prostate cancers that use hormones to grow.
- **Immunotherapy to treat cancer:** immunotherapy is a type of cancer treatment that helps your immune system to fight cancer.
- **Radiation therapy:** Radiation therapy is a type of cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumors.
- **Stem cell transplant:** stem cell transplant procedure for blood forming stem cells and cancer patients who have had their eyes destroyed by a very high dose of chemotherapy or Radiation therapy.
- **Surgery:** Surgery is a procedure in which a surgeon removes cancer from your body.
- **Targeted therapy:** targeted therapies a type of cancer treatment the targets the changes in Cancer cells that help them grow and divide and spread.
- **Hyperthermia:** hyperthermia is a type of treatment in which body tissue is heated to as high as 113-degree Fahrenheit to help damage and kill cancer cells with little or no harm to normal tissue. Hyperthermia to treat cancer is also called thermal therapy, thermal ablation or thermotherapy.
- **Photodynamic therapy:** photodynamic therapy uses a drug that is activated by light called photosensitizer or photosensitizing agents to kill cancer cells. The light can come from a laser or other sources such as Photodynamic therapy is also called PDT. Photodynamic therapy is most often used as a local treatment which means it reaches specific part of the body.

Radiation therapy working against cancer: at high doses Radiation therapy kills cancer cells or slows their growth by damaging their DNA.^[14] Cancer cells whose

DNA is damaged beyond repair stop dividing or die^[15]. When the damaged cells die, they are broken down and removed by the body.^[16] Radiation therapy takes days or weeks of treatment before the DNA is damaged enough for cancer cells to die. Cancer cells keep dying for weeks or months after radiation therapy ends.^[17]

Radiation therapy depends upon^[18]

- Type of cancer
- Size of tumor
- Tumor location in the body
- The distance between the tumor and the normal tissue that are sensitive to radiation
- General Health and Medical history
- One or more cancer treatments
- Radiation receiving person age and other conditions.

Radiation therapy method^[19]

- Before treatment: CT and simulation.
- 2D beams using linear accelerator machines from several angles.
- Aimed at tumor and sometimes the draining lymph node.
- Facilitated by MRI and PET scanning.
- Dose (measured in Gy) – Fractionated.
- Typical dose – 2Gy fractions 5 times a week over a 6–7-week period.

When is radiotherapy used^[20]

- **Adjuvant**
 - Following BCS (Breast conservative surgery)
 - Following mastectomy
- **Neo-Adjuvant**
 - Large fungating lesions
- **Radical**
 - Primary incision not possible.
- **Palliative**
 - Large fungating lesions
 - Metastatic diseases.
- **Adjuvant** – adjuvant therapy treatment after tumor removal. It can help prevent cancer through returning and kills off remaining cancerous cells. The treatments can weaken the person further due to unpleasant side effects.
- **Neo-Adjuvant** – Neo-Adjuvant Therapy is treatment before tumor Removal. It helps shrink the size of tumors making them easier to cut out. Delay in surgical removal of the tumor could mean the cancer spread.
- **Radical** - The aim of radical radiotherapy is to shrink and control the growth of your tumor, with intent of curing your cancer and prolonging your life.
- **Palliative** - The aim of palliative radiotherapy is to relieve symptoms of the disease, without attempting to cure the patient. It is only appropriate for patients with incurable disease and a short life expectancy. This approach is useful for palliation of metastases, especially in brain or skin.

Types of Radiation therapy

External beam radiation: external beam Radiation therapy comes from a machine that aims radiation at the cancer^[21] The machine is large and noisy.^[22] External beam radiation therapy is a local treatment which star gets the specific part of the body. For example, if you have cancer in your lungs, you will have radiation only to your chest not your whole body.^[23]

Types of beams used in radiation therapy^[24]

- **Photon:** Photon beams can reach tumors deep inside the body and travels in body.^[25] Photon beams scatter little bits of radiation along their path. These beams do not stop once they reach the tumor but go into normal tissue past it.
- **Protons:** protons are particles with a positive charge. Like Photon beams Proton beams can also reach tumors deep inside the body but Proton beams do not scatter radiation on their path through the body and they stop once they reach the tumor.
- **Electrons:** electrons are particles with negative charge. Electron beams cannot travel very far through body tissues. The use is limited to tumors on the skin or near the surface of the body.^[26]

Types of external beam Radiation therapy

- **3D conformal Radiation therapy:** it is a common type of external beam Radiation therapy and it uses images from CT, MRI and PET scans to precisely plan the treatment area which is a process called simulation.^[27] A computer program is used to analyze the images and to design radiation beams that conform to the shape of the tumor. 3D conformal radiation conforms to the shape of the tumor by delivering beams from many directions. The precise shaping makes it possible to use higher dose of radiation to the tumor while sparing normal tissue. Most people have treatment once a day like Monday to Friday.^[28]
- **Intensity-modulated Radiation therapy (IMRT):** it is a type of 3D conformal Radiation therapy and radiation beams are aimed at the tumor from several directions. It uses many smaller beams and 3D conformal and strength of the beams in some areas can be changed to give higher doses to certain parts of the tumor.
- **Image guided Radiation therapy (IGRT):** IGRT is a type of IMRT which uses imaging scans not only for treatment planning before radiation therapy sessions but also during radiation therapy sessions. During treatment patient will how repeat it scans such as CT, MRI or PET scans. These scans are processed by computer to detect changes in the tumor size and location.^[29] The repeated imaging allows for the position for the radiation dose to be adjusted during the treatment if needed. These adjustments can improve the accuracy of treatment and helps spare normal tissue.
- **TomoTherapy:** TomoTherapy is a type of a method that uses a machine that is combination of a CT

scanner and external beam radiation machine. TomoTherapy machine takes images of the tumor right before the treatment sessions to a low for very precise tumor targeting and sparing of normal tissue. It rotates around the patient during the treatment and delivering radiation in a spiral pattern slice by slice. TomoTherapy is better at sparing normal tissue than 3D conformal Radiation therapy.

- **Stereotactic radiosurgery:** stereotactic radiosurgery is the use of focused and high energy beams to treat small tumors with well-defined address in the brain and central nervous system. This option of surgery is too risky due to the age or other health problems or if the tumor cannot safely be reached with surgery.^[30] Gamma knife is a type of stereotactic surgery. The patient will be placed in a head frame or some other device to make sure the patient does not move during the treatment. In stereotactic surgery many small beams of radiation are aimed at the tumor from different directions. Each beam has very little effect on the tissue it passes through but a precisely targeted dose of radiation is delivered to the site where all beams come together. The treatment is given only in one dose.^[31]
- **Stereotactic body Radiation therapy:** stereotactic body Radiation therapy is smaller to stereotactic radiosurgery but used for small and isolated tumors outside the brain and spinal cord like in the liver or lung.^[32] Stereotactic body Radiation therapy uses special equipment to hold the patient still during the treatment and delivers highly precise beams to a limited area. Stereotactic body radiation is usually given in one or more than dose up to 5 doses.^[33]

Different ways of delivering the total radiation dose

- **Accelerated fractionation:** which is treatment given in larger daily or weekly doses to reduce the number of weeks of treatment.
- **Hyper fractionation:** which is smaller dose than usual dose of radiation given more than once a day.
- **Hypofractionation:** which are larger doses given once a day or less often to reduce the number of treatments.

Internal Radiation therapy: internal Radiation therapy is a treatment in which a source of radiation is put inside the body and the radiation source can be solid or liquid. Internal Radiation therapy with the solid source is called brachytherapy. In this type of treatment seeds, ribbons or capsules that contain irradiation source are placed in the body, in or near the tumor. Internal Radiation therapy with liquid source called systemic therapy. Systemic means the treatment travels in the body tissues throughout the body and seeking out and killing cancer cells. Systemic therapy by swallowing through a vein via an IV Line or through an injection is received.

Techniques for placing brachytherapy include

- **Interstitial brachytherapy:** in which the radiation source is placed within the tumor and the technique is used for prostate cancer.
- **Intracavitary brachytherapy:** in which the radiation source is placed within a body cavity or a cavity created by surgery. Radiation can be placed in the vagina to treat Cervical or endometrial cancer
- **Episcleral brachytherapy:** in which the radiation source is attached to the eye and this technique is used to treat Melanoma of the eye.

Types of brachytherapy^[34]

- **Low dose rate implants (LDR):** in this type of brachytherapy the radiation source stays in the place for 1 to 7 days.
- **High dose rate implants (HDR):** in this type of brachytherapy the radiation source is left in place for just 10 to 20 minutes at a time and then taken out.
- **Permanent implants:** after the radiation source is put in place the catheter is removed and the implants remain in the body for the rest of the life but the radiation gets weaker each day. As the time goes on almost all the radiation will go away.

Side effects of radiation therapy.

Part of the body being treated	Possible side effects
Brain	Hair loss, nausea and vomiting, skin changes, headache, blurry vision
Breast	Hair loss, skin changes, swelling, tenderness, fatigue ^[35]
Chest	Fatigue, hair loss, mouth changes, skin changes, taste changes, difficulty in swallowing, cough and shortness of breath
Head and neck	Fatigue, hair loss, skin changes, trouble swallowing, taste changes, less active thyroid gland
Pelvis	Diarrhea, fatigue, hair loss, nausea and vomiting, Sexual problems in men, fertility problems in men and women, skin changes, urinary and bladder changes
Rectum	Diarrhea, fatigue, hair loss, Sexual problems and fertility problems in both men and women, skin changes and urinary bladder changes ^[36]
Stomach and abdomen	Diarrhea, hair loss, nausea and vomiting, skin changes and urinary changes. ^[37]

Cisplatin chemotherapy^[38] cisplatin has been used as first-line therapy for several cancers including testicular, ovarian, cervical, head and neck and small cell lung cancer^[39] either alone or in combination with other anticancer agents.^[40] It is also used as adjuvant therapy following with surgery or radiation.^[41] Cisplatin is a cytotoxic agent.^[42] The antitumor activity of cisplatin is believed to be due to its interaction with chromosomal DNA.^[43,44] Cisplatin or Cis diamine dichloro Platinum(II) is a neutral square planar coordination Complex of divalent Pt.^[45] Thus is configuration is required for its antitumor activity.^[46] The platinum atom of cisplatin forms bonds with interstrand crosslinks.^[48,47] The interstrand and intrastrand cross-linked disrupt the structure of the DNA.^[49] This alteration in the structure is recognized by the cellular proteins to repair cisplatin induced DNA.^[50] Increased repair of cisplatin induced DNA damage has been associated with cisplatin resistance.^[51,52]

Pharmacokinetic data

- Bioavailability - 100% intravenous
- Protein binding - >95%
- Elimination half – life – 30-100 hrs.
- Excretion – renal.

Cisplatin dose: 50 to 70 mg /m² IV per cycle once every three to four weeks depending on the extent or prior exposure to Radiation therapy or prior to chemotherapy.

Pretreatment hydration - pretreatment hydration with 1 to 2 litres of fluid infused for 8 to 12 hours prior to cisplatin injection dose is recommended. The drug is then diluted into litres of 5% dextrose in ½ or 1/3 normal saline containing 37.5 G of mannitol, and infused for 6 to 8 hour period. Adequate hydration and urinary output must be maintained during the following 24 hours.

Caution: repeat course of cisplatin should not be given until the serum creatinine is below 1.5 mg per 100ml. A repeat course should not be given until circulating blood elements are at an acceptable level(platelets > 1lac/mm³, WBC >4000/mm³). Subsequent doses of cisplatin should not be given until and audiometric analysis indicates that auditory acuity is within normal limits.

Cisplatin resistance: cisplatin combination chemotherapy is the cornerstone of treatment of many cancers. Initial Platinum responsiveness is high but the majority of Cancer patients will eventually relapse with cisplatin resistant disease. Mini mechanism of cisplatin resistance have been proposed including changes in cellular uptake and efflux of the drug, increased detoxification of the drug and inhibition of apoptosis and increase a DNA repair. Drug paclitaxel may be useful in the treatment of cisplatin resistant cancer.

Common side effects of cisplatin:^[53] Risk of infection(the treatment can reduce the number of white blood cells in the blood)^[54] bruising and bleeding, anemia, feeling sick, loss of appetite, changes in taste,^[55]

nephrotoxicity, Ototoxicity, patients often develop resistance.^[56]

Cisplatin combination with radiation therapy:^[57] the combination of cisplatin and ionizing radiation treatment represents a common modality for treating a variety of cancers.^[58] These two agents provide considerable scenery during treatment all the mechanism of this energy remains largely different.^[59] A clear synergistic interaction between cisplatin and ionizing radiation is observed in cells proficient in non-homologous end joining catalyzed repair of DNA double-strand breaks.^[60,61]

CONCLUSION

Cancer is a multifactorial disease. Due to this reason the treatment of cancer should take into consideration all factors and not just the physical factor. Patients suffering with cancer have more treatment choices. Combination of Radiation therapy and cisplatin chemotherapy having the best results in treatment of squamous cell carcinoma. Early detection of cancers increases the chance of the cure. In clinical aspect Radiation therapy goal achieved by local control with less toxicity in small sized tumor and well capsulated tumor. Also, chemotherapy may be an alternative modernity with radiation therapy for high intermediate risk and high-risk endometrial cancers.

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