

**RADIATION THERAPY IN CANCER DIAGNOSIS AND TREATMENT**

Mahadev Govindrao Tate\* and Gayatri Mohan Saini

India.

\*Corresponding Author: Mahadev Govindrao Tate

India.

Article Received on 19/02/2019

Article Revised on 11/03/2019

Article Accepted on 01/04/2019

**ABSTRACT**

Radioisotopes are unstable atomic isotopes that give off radiation spontaneously. They can be measured by a suitable apparatus at amounts as small as one-billionth of a gram. Thus, they can be safely used in small amounts as in the body.<sup>[3]</sup> Today, radioisotopes are used both diagnostically and therapeutically in medicine. Radiation therapy is used against many types of cancer. About 60% of cancer cases require radiation therapy. Carcinomas are an example of a type of cancer that often has high division rates. These types of cancer tend to respond well to radiation therapy. Radiation therapy is delivered in a 'Radiation oncology' department. More than 14 million new cases of cancer are diagnosed globally each year; radiation therapy (RT) has the potential to improve the rates of cure of 3.5 million people and provide palliative relief for an additional 3.5 million people.<sup>[12]</sup> The success rate of radiation therapy is near about 80% for many cancers.

**KEYWORDS:** Radioisotopes, Radiation therapy (RT).**INTRODUCTION**

Radioactive compounds used in nuclear medicine for diagnosis or treatment has great potential for the treatment of cancer, especially for cancer cells that have migrated from primary tumors to lymph nodes and secondary organs such as bone marrow. The most famous type is probably gamma ray irradiation by radioactive cobalt-60. At high doses, radiation therapy kills cancer cells or slows their growth by damaging their DNA. Cancer cells whose DNA is damaged beyond repair stop dividing or die. When the damaged cells die, they are broken down and removed by the body.

In systemic radiation therapy drug is given either orally or through intravenous(IV) route.

They travel in the blood throughout the body. The antibody makes them attach to the cancer cells. They then give off their radiation and kill the cancer cells. systemic radiation uses an unsealed radioactive substance that goes through your whole body, some radiation will be in your body for a few days until your body has had a chance to get rid of it. You may need to stay in the hospital for 1 or 2 days.

The amount of radiation and the type needed depends on each individual case, taking into account tumor size, the stage of the cancer, tumor location, health of the patient, method of radiation delivery, and total dose. If tumor are treated at early stage by using radioactive therapy that time rate of successful treatment is high. To check the

effectiveness of the treatment, doctors can use imaging tools like CT scans.<sup>[13]</sup>

**Diagnosis of Cancer by Using Radioisotopes**

Optical imaging is an important field in cancer diagnostics because it allows noninvasive diagnosis of tumors.<sup>[3]</sup> Optical imaging scans are used to detect cancer and monitor its progression and metastases.

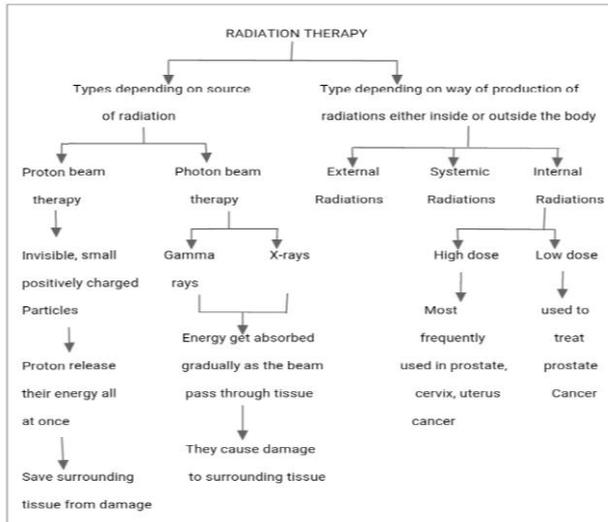
CT (computed tomography), MRI (magnetic resonance imaging), SPECT (single-photon emission computed tomography), and PET (positron emission tomography) imaging modalities are preferred methods of optical imaging for cancer detection because they are three-dimensional. But all these methods are less sensitive for small number of cancer cells and therefore they have less resolution power. Thus, contrast agents and radiotracers are useful methods of improving imaging sensitivity.<sup>[5]</sup> Radiotracers that target specific tumors display localized signal at that tissue, revealing location and size of the tumor.

Technetium-99m is referred to as the "workhorse of modern medical imaging", because it accounts for about 80% of the world's radioactive isotopes in nuclear medicine, 90% of which is used in diagnosis scans. It is an ideal element for nuclear medicine because it has a half life of 6 hours. It emits gamma rays. Gamma rays are massless and easily detected outside of the body. In addition, Technetium-99m has a volatile chemistry that allows it to easily be incorporated in biologically active

substances that target an organ or tissue of interest. Medical scans like SPECT then pick up the glow of the radioisotope and its localization. These tests are used to check how well blood is flowing to heart muscles, to spot whether cancers have spread through bones and to assess blood flow in the brain.<sup>[15]</sup>

## Types of Radiation Therapy

### →Types Depending on Source of Radiation



### • Photon Therapy

#### Photon radiation therapy are of two types

» Gamma rays: produced by the breakdown of radioactive isotopes of elements such as Cobalt- 60 and radium.

» X-rays: originate from machines that excite electrons using cathode ray tubes or linear accelerators.

These high energy particles are produced by a machine called a “linear accelerator” or “linac.” The machine is used to target photon beams at tumors inside the body.<sup>[11]</sup> Photon therapy can also damage healthy cells in the body.<sup>[17]</sup> Photons such as X-rays are delivered as waves which do not have any charge.

They pass through the body and release energy all along the way. The energy in photon beams ( like X-rays) gets absorbed gradually as the beams pass through tissues. Because of this, they cause damage to the tissues they pass through as they travel towards the targeted tumor.

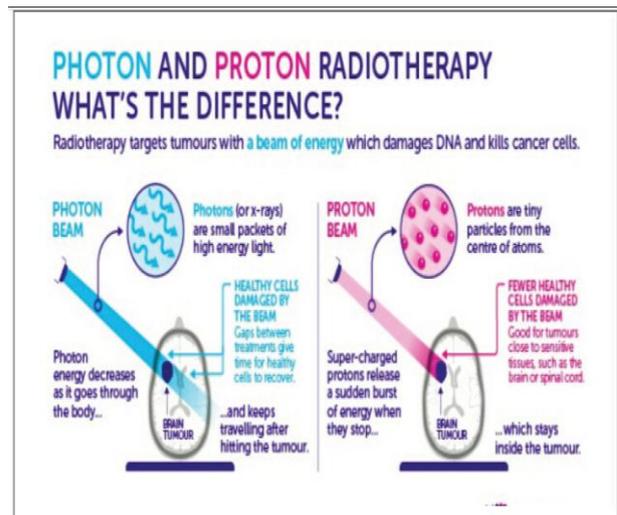
### • Proton Beam Therapy

Proton therapy is a radiation therapy that uses tiny particles called protons. Protons are excellent cell killers. Proton beam therapy is better than photon therapy because it does not damage the healthy tissues. Therefore, a higher dose of radiation can be targeted at the tumor without affecting many normal healthy cells. Protons are “accelerated” and released in beams by a machine called a cyclotron or a synchrotron. The initial speed of the charged particles determines how deep in the body it will travel before releasing its energy, while

the strength of the beam (how powerful or energetic it is) determines the dosage of radiation delivered at the point of tumor.

A proton is an invisibly-small (sub-atomic) positively-charged particle. How deeply a proton travels into the body depends on the speed of the proton when it leaves the machine.

Protons release their energy all at once. They do not damage cells they pass through until they release their energy in a single burst. Because all the radiation energy is targeted at the tumor, little energy is released into the tissues beyond the tumor. This saves the surrounding tissue from any damage.<sup>[9]</sup>



### →Types Depending on Way of Production of Radiations Either Inside or Outside The Body

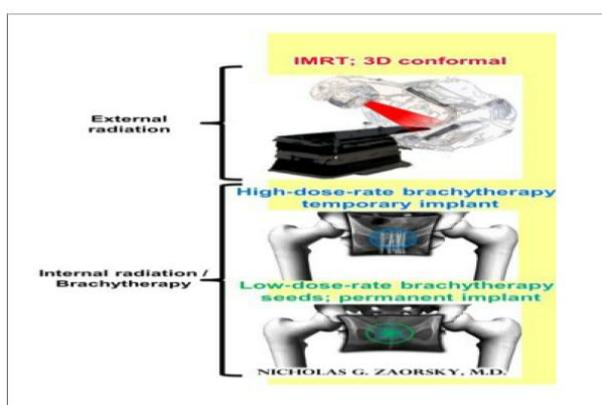
**1) External radiation:** In this type of therapy uses high energy rays that are delivered to the tumor by a machine. The common types of external radiation are Intensity Modulated Radiation Therapy (IMRT) and Three Dimensional Conformal Radiation Therapy (3D-CRT). With conventional fractionation of EBRT, the patient receives single small dose, 15 minutes per day, 5 days per week, for about 2 to 8 weeks (the overall treatment time depends on the goal of therapy and other treatments involved). On the other hand, with hypofractionated techniques (e.g. stereotactic body radiation therapy [SBRT], stereotactic radiosurgery [SRS]), a large dose is delivered to the tumor in five fractions or less.

**2) Internal radiation or brachytherapy:** Radioactive “seed” or “pellet” are use which is placed inside the body, in or near the tumor; the radioactive source releases energized particles that target and kill the tumor cells. Most often, the source of the radiation is inserted into the body using a needle or a catheter. Different imaging tests, including CT scans and ultrasounds are used to choose the exact position to place the radiation sources in the body.

The doses of radiation used in brachytherapy are designed to target all of the cancer but to cause as little damage as possible to nearby normal tissues. Some side effects of brachytherapy are pain, swelling and bleeding at the location where the radioactive pellets are inserted.<sup>[20]</sup>

Prostate, Cervical, Uterine, Breast, Lung, Rectal, Eye, Skin type of cancers are most of the time treated with brachytherapy. Depending on the cancer, BT is typically given as either high- dose rate (HDR) or low-dose rate (LDR).

**3) Systemic radiation:** It involves introducing radioactive chemicals into the body, usually through the mouth or blood vessels (IV injection).



**Procedure for Radiation Therapy:** Depending on type of therapy procedure is change as per requirements.

- **External Radiation Therapy:** A patient receiving this radiation therapy will lie down on a table with the linac moving around them to send out the photon beams from different directions. A treatment session is normally between 10 min to 30 min long. This is typically an outpatient procedure taking place 5 times per week.<sup>[10]</sup> Cobalt units contain radioactive cobalt sources in the head of the unit that emit photons with a mean energy of 1.25 MeV.

- **Internal Radiation Therapy:** The patient is usually under general anesthesia during any type of BT procedure. In High Dose Radiation (HDR)-BT, a machine automatically releases a single small radioactive source (usually Iridium 192) through the needle inserted at specific positions delivering a high dose of radiation for a few minutes in "fractions" over the course of 1 to 10 days. The HDR-BT machine allows a physician to control the position where the radioactive source stops for a certain period of time (i.e. the "dwell position" and "dwell time," respectively).

Low Dose Radiation (LDR)-BT consists of the permanent insertion of enclosed, encapsulated sources (i.e. "seeds," usually Iodine or Palladium), delivering a low dose of radiation that reduces over the time course of

months. During the procedure, radioactive seeds (each only a few millimeters in size) are inserted directly in the tumor. The LDR-BT implantation is done once over the course of about an hour.

**Once a decision to treat a patient has been made**

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**Prescription**

The first step is completion of the radiation prescription, which indicates the exact part of the body to be treated, as well as the dose/fractionation schedule, including the total radiation dose to be delivered in how many fractions, at what intervals, and in what overall time period.

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**Planning**

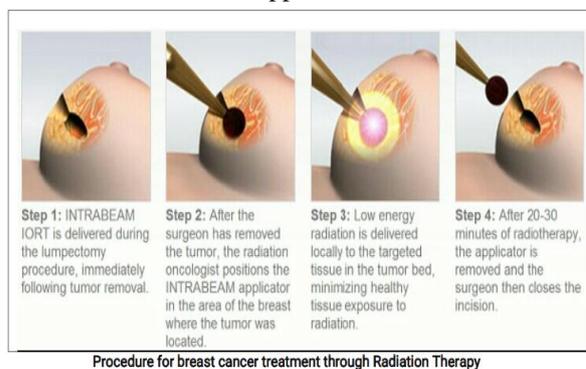
The team develops a treatment plan and proceeds with delivery. (The plan is based on accepted clinical guidelines that describe the indications for RT).

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**Treatment Delivery**

Once the treatment plan is developed by a medical physicist and dosimetrist and reviewed and approved by a radiation oncologist, the treatment can begin. The target tissues irradiated.

» During each session, specific verification steps are taken before the dose is applied.



Procedure for breast cancer treatment through Radiation Therapy

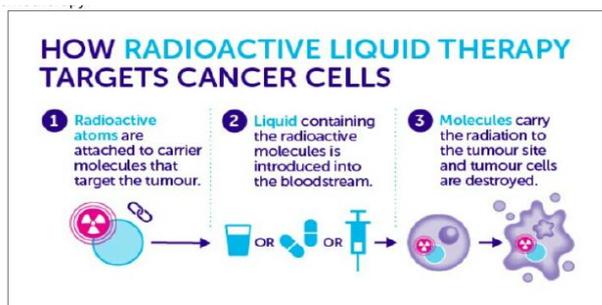
**Requirements for Radiation Therapy:** RT is delivered in a specially designed facility that contains specialized equipment for imaging, treatment planning, and radiation delivery. Modern RT department includes Waiting areas, Examination rooms, Imaging suites with simulators/ CT-simulators, Computer planning workrooms, Shielded treatment rooms for linear accelerators. Additional support space is required for a physics testing laboratory, equipment storage, and dedicated environmentally controlled computer server rooms.

Radionuclide	Half-life (days)	Decay particle	Tissue penetration (mm)
Radium-223	11.4	Alpha	<0.1
Strontium-89	50.5	beta	5.5
Samarium-153	1.9	beta, gamma	2.5
Rhenium-186	3.8	beta, gamma	4.5
Rhenium-188	7	beta, gamma	11.0

**Mechanism of Radiation Therapy:** Radiation therapy uses high-energy particles or high-energy waves to kill cancer cells. Cells grow and reproduce in order to create new cells and replace cells lost to damage and aging. Cancer cells reproduce faster than normal cells and lack the controls found in normal cells. The high energy particles (or waves) kill cancer cells by causing damage to their genetic information (DNA). DNA contains the information used to control cell growth and division.<sup>[7]</sup>

Radiation is a localized therapy, the high energy beams are targeted directly at the cancer. Efforts are made to avoid as many healthy cells as possible. The waves stop certain internal functions of the cell that are involved in cell division, so the cells eventually die. The cells do not die immediately; cell death occurs when the cells try to divide but fail. This is called abortive mitosis.<sup>[16]</sup>

The degree of tumor shrinkage depends on the balance between cell production and cell death. To prevent regrowth of the tumor radiation is often coupled with surgery and/or chemotherapy.



**Precautions:** Some precautions should be taken to reduce the damage of healthy cells and to achieve high degree of damage to tumor cells. To achieve this balance physicians take following precautions.

- 1) Find several different pathways to the tumor, so that regions of healthy cells don't get exposed to the photon beams more than necessary.
- 2) Break down the total dose of therapy into smaller amounts delivered over time through multiple treatment sessions.
- 3) Target the photon beam to tumors by choosing pathways that are not too close to organs that could be damaged.

### Advantages of Radioactive Therapy

1. One of the advantages of using radioisotopes in medicine is that the radiation from gamma rays which is the Co-60 is used in the diagnosis and treatment of thyroids, this type of treatment is more effective than other methods like chemotherapy.

2. The (P32) radio phosphorus and the I-123 are ideal in the treatment and diagnosis of cancer; that is leukemia and tumours, detecting this early by the use of radioisotopes helps in early medical treatments.

3) With the advantage of radioisotopes in medicine; the diagnosis, tracing and treatment of medical illness are profound and put into practise with less expenses going on to on research and studies.

4) The use of radioisotopes in medicine holds an advantage to patients. Through medical sterillisation patients don't get infected and thus making it useful in the health department.

5) Deathof a large proportion of cancer cells within the entire tumor (there are minimal, if any, cancer cells are left behind in small tumors; thus, radiation alone may be used to cure certain small tumors).

6) In case of external radiation therapy relative safety for the patient (radiation can be delivered from outside of the body and focused on the tumor, is painless, and generally does not require anesthesia).

7) Organ preservation (e.g. not removing a breast, larynx, or part of the gastrointestinal tract, which would have significant negative impact on a patient's quality of life).

### Disadvantages of Radioactive Therapy

1) Radioisotopes are much expensive and not every hospital can pay the price for consuming them. They are also inevitably hard to store since they continuously emit radiations which is hazardous.

2) One of the problems that radioisotopes cause is 'genetic mutation'.

3) The major demerit of using radioisotopes in nuclear medicine is that it has a negative impact on health. Tissues are damaged, leading to skin burns, nausea,diseases such as leukemia and lung cancer, this eventually leads to death.

4) Radioisotopes require nuclear reactors for production and this may not be easy to purchase because they are expensive.

5) The radioactive wastes from using radioisotopes can not simply be dumped into any place, they need disposals that are not gonna have an effect on omitting

radiation to people or to the ozone layer causing a green house effect.

6) If we use radioisotopes in excess amount then enzyme can denature and disruption of protein synthesis can occur, thus leading to the malfunctioning of an enzyme or a protein.

7) if radioisotopes are exposed to a living thing in big quantities, it will have an effect on this organisms immunity and resistance, depending on the type of radioisotope released on to the organism.

8) Most other malignant cancers are not considered curable with radiation because they are difficult to detect early enough and/or they have a much higher growth rate. Tumors found in especially sensitive tissue cannot be treated with the large dose of radiation necessary to kill the tumor.

9) Radiation therapy alone is not usually successful against highly metastatic tumors. At this stage combination therapy is require.

10) Radioactive materials can leave your body through saliva, sweat, blood, and urine and that makes these fluids radioactive therefore patient's safety is much more important during this type of therapy.

11) Increases risk of postoperative complications.

12) Inconvenience of radiation therapy (e.g. in some cases it must be delivered daily, 5 days per week, for 1-2 months).

13) If a cancer comes back in the same area that was treated before, you may or may not be able to receive radiation to that same location.

**Applications:** After Roentgen's discovery of X-rays in 1895, ionizing radiation was applied to the treatment of cancer, with remarkable results. Carefully controlled doses of ionizing radiation induce damage to the DNA in cells, with preferential effects on cancer cells compared with normal tissues, providing treatment benefits in most types of cancer and saving lives.

- High Dose Rate (HDR)-BT is most frequently used in cancers of the prostate, cervix, uterus; it is sometimes used for cancers of the lung and breast.

- Low Dose Radiation (LDR)-BT is most often used to treat prostate cancer.

#### Side Effects of Radiation Therapy

In case of RT two types of side effects are found i.e.

- 1) Short term effects.
- 2) Long term effects.

- The skin over the site of radiation may get red and/or sore.

- Development of a second cancer, caused by the radiation therapy, is relatively uncommon, but can occur. How likely it is to happen depends on a several things, including the site being treated, and the age of the patient.

- The most common side effect is fatigue (in part due to energy expended in replacing normal cells killed in the process).

- Effects specific to the area of treatment, such as urinary problems, nausea, vomiting, and diarrhea, tissue inflammation, such as esophagitis, pneumonitis, and hepatitis.

- Rarely, a drop in the number of white blood cells or platelets.

Not all of the above examples are likely or even possible with all types of radiation therapy. The likelihood of getting any one of the longer-term side effects depends largely on the individual.

**Challenges in front of Radiation Therapy(rt):** RT is now recognized as an essential element of an effective cancer care program throughout the world. RT is one of the more cost-effective cancer treatment modalities, despite the need for substantial capital investment in the facilities and equipment. RT requires a specially trained team of professionals that includes radiation oncologists to prescribe the dose; medical physicists, trained to commission and maintain the equipment and develop treatment plans.

**Combination Therapy:** There is ongoing discussion regarding the relative benefits of pre-operative and post-operative radiation. Both have their advantages and disadvantages. So combination therapy is the best option for Cancer treatment. Each patient's case must be assessed individually to determine the best treatment method. One type of therapy can sometimes make a tumor more vulnerable to a second type. Combining two or more types of treatments - such as surgery, radiation, and chemotherapy - may be more effective than a single therapy alone.

Anti-cancer drugs enhances efficacy compared to the mono-therapy approach because it targets key pathways in a characteristically synergistic or an additive manner. This approach potentially reduces drug resistance, while simultaneously providing therapeutic anti-cancer benefits, such as reducing tumour growth and metastatic potential, arresting mitotically active cells, reducing cancer stem cell populations, and inducing apoptosis.

The use of more than one type of therapy in treating a patient, is a hallmark of cancer treatment. In many cases,

combination therapy not only increases the chances of a cure or long-

-term remission, but also reduces damage to vital organs and tissues more than a single approach.

**Example:** Adjuvant (“helper”) radiation therapy given before surgery for rectal cancer to reduce the risk of recurrence, increase the likelihood of cure, and reduce the likelihood that the patient will require a permanent colostomy.

**Advancement in Radiation Therapy:** RT has undergone tremendous progress over the years, realising technological developments that have revolutionised its clinical use. Radiation therapy is a type of cancer treatment that uses beams of intense energy to kill cancer cells. The advent of sophisticated treatment delivery techniques has made it necessary to develop advanced Treatment Planning. The advances in technology have led to an escalation of the prescription dose or a change in the number of fractions.

In recent years, increased attention has been paid to the radiobiological optimisation of the treatment plan, using TCP and NTCP models. Dose–volume optimisation techniques are a mainstay of current TPSs, the biological optimisation used in IMRT planning is able to reduce radiation-induced toxicity. Advanced inverse-planning techniques have led to the development of more automated approaches, plan optimisation is still a very time-consuming task with output varying greatly according to the experience of the operator.

Combining advanced techniques of functional MRI, including T2 weighted (T2W), dynamic contrast enhanced and diffusion weighted imaging (DWI), improves visualisation and the accurate detection of intra-prostatic lesions and differentiates between low and intermediate/high-grade tumor.

IGRT(Image-guided radiotherapy) not only makes it possible to improve the accuracy of the treatment by minimizing the inter-fractional position uncertainties, but it is also able to monitor systematic changes in the shape and position of tumour volume and of normal tissue (weight loss and tumour regression), which means that the plan can be suitably modified.

## CONCLUSION

Cancer is projected to become the number one cause of death across the globe in the next 20 years. By exploring all the aspects will we manage to produce individualised radiation therapy with better target delineation, avoidance of normal tissue, dose escalation, dose fractionation and better prediction of treatment response. The evidence demonstrates that more than 40 percent of patients with cancer would benefit from RT. The use of modern radioisotopes in selected patients is associated with improvements in overall survival, pain control, and quality of life.

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