Review Article

Radiotherapy

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ABSTRACT

Radiotherapy is also called as radiation therapy that uses ionizing radiation for the treatment of cancer due to its ability to control cell growth. It is used in synergistic with other treatments such as chemotherapy and surgery during the treatment plan. Radiotherapy goals are to control symptoms for incurable cancers, shrink tumor size, restrict or destroy malignant cells and also prevent tumor recurrence. It can also be used as a palliative or a therapeutic treatment. The accurate treatment fixation depends on the type of tumor, location, stage, and the general health of the patient. It is not only used for the treatment of cancer but also has its application witnessed on non-malignant conditions.

KEY WORDS: Radiotherapy, Radiology, Radiations

INTRODUCTION

Radiotherapy is also called as radiation therapy that uses ionizing radiation for the treatment of cancer due to its ability to control cell growth. It is used in synergistic with other treatments such as chemotherapy and surgery during the treatment plan. Radiotherapy goals are to control symptoms for incurable cancers, shrink tumor size, restrict or destroy malignant cells and also prevent tumor recurrence. It can also be used as a palliative or a therapeutic treatment. The accurate treatment fixation depends on the type of tumor, location, stage, and the general health of the patient. It is not only used for the treatment of cancer but also has its application witnessed on non-malignant conditions.

The extent of response of the cancer cells to the radiation is termed as radiosensitivity. Based on the above property malignant cells can be classified as radiosensitive or radioresistant. Leukemia and lymphomas are highly radiosensitive whereas epithelial cancers are moderately sensitive and melanomas and renal cell cancer are termed to be radioresistant. Radiosensitivity is affected by various parameters such as size of the tumor and by administration of certain drugs like cisplatin, nimorazole enhances the radiosensitivity of the tumors by various inhibitory methods. The complexity of the tumor, large tumor responds less to radiation than small or microscopic tumors. The cell cycle phase is the important phase as the radiation kills those cells that are actively dividing. There is no immediate response of the radiation on the cells that are in the resting stage (G0) or dividing less. The amount and type of radiation that reaches the cell and the speed of cell growth affect how efficient and fast the cell will be destroyed.[1]

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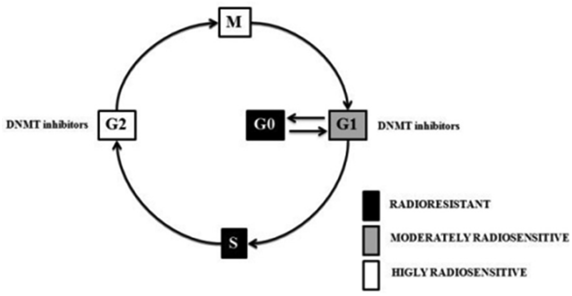

G0 = Cell rests (it's not dividing) and does its normal work in the body
G1 = RNA and proteins are made for dividing
S = Synthesis (DNA is made for new cells)
G2 = Apparatus for mitosis is built
M = Mitosis (the cell divides into two cells).

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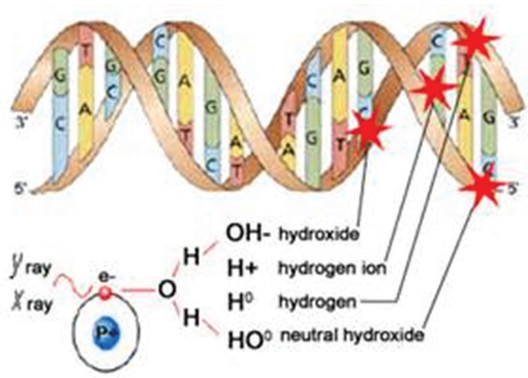
MECHANISM OF ACTION

Radiation therapy works by damaging the DNA of cancerous cells. This damage is caused by two types of energy, photon or charged particles. It is either direct or indirect ionization of the atoms which make up the DNA chain. Indirect ionization happens by ionizing water to form free radicals which cause the DNA damage. Each cell has the natural ability to repair it's DNA damage; hence, single-stranded DNA damages are much easier to repair than double-stranded DNA damage. Double-stranded DNA damage can cause complex problems such as chromosomal abnormalities and genetic deletion leading to an increase in the probability of cell death. Oxygen is a potent radiosensitive and hence when solid tumors can create a state of hypoxia which increases it's radio-resistant property increases. Charged particles have an antitumor effect independent of oxygen supply and act directly on the double-stranded DNA to cause damage. They also reduce the effect on the surrounding tissues as they are size specific and stay focused on the tumor.[2,3] The amount of radiation in photon therapy is measured in gray (Gy), and it varies depending on the type and stage of cancer that is being treated. Fractionation of the dose is important to avoid overexpose, and scheduling is formidable to prevent over damage to the surrounding normal tissues.

The dose of radiation absorbed correlates directly with the energy of the beam. An accurate measurement of absorbed dose is critical in radiation treatment. The deposition of energy in tissues results in damage to DNA and diminishes or eradicates the cell's ability to replicate indefinitely.[4]



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PRINCIPLE

Ionizing radiation is the energy sufficiently strong to remove an orbital electron from an atom. High energy photons are the commonly used forms in practice today. Photon's are classified into two based on their origin - gamma rays and X-rays. Gamma rays are released from the nucleus of a radioactive atom whereas X-rays are created electronically in a linear accelerator. Inverse square law governs the intensity of the X-rays. Photon-tissue interaction is of major concern.[5] There are three types of interactions seen which describe the absorption of photons by the tissues.

Photoelectric Effect

In this process, an incoming photon undergoes a collision with a tightly bound electron. The photon transfers practically all of its energy to the electron and ceases to exist. The electron departs with most of the energy from the photon and begins to ionize surrounding molecules. This interaction depends on the energy of the incoming photon, as well as the atomic number of the tissue.

Compton Effect

The Compton effect is the most important photon-tissue interaction for the treatment of cancer. In this case, a photon collides with a "free electron," that is, one that is not tightly bound to the atom. Unlike the photoelectric effect, in the Compton interaction, both the photon and electron are scattered. The photon can then continue to undergo additional interactions, albeit with lower energy. The electron begins to ionize with the energy given to it by the photon.

Pair Production

In this process, a photon interacts with the nucleus of an atom, not an orbital electron. The photon gives up its energy to the nucleus and, in the process, creates a pair of positively and negatively charged electrons. The positive electron (positron) ionizes until it combines with a free electron. This generates two photons that scatter in opposite directions.

Electron absorption in human tissue is greatly influenced by the presence of air cavities and bone. The dose is increased when the electron beam passes through an air space and is reduced when the beam passes through bone. The most common clinical uses of electron beams include the treatment of skin lesions, such as basal cell carcinomas.[4]

TYPES

There are three major divisions of radiation therapy which are based on the position of the radiation source - external beam radiation therapy or teletherapy, brachytherapy or sealed source radiation therapy, and systemic radiation therapy or unsealed radiation therapy. The position of the radiation source in external beam radiation therapy is outside the body, in Brachytherapy the sealed radioactive source is placed promptly placed in the area under treatment and in system radioisotopes it is given by infusion or oral ingestion. Brachytherapy can use temporary or permanent placement of radioactive sources which minimizes the radiation exposure to the health-care personal, and it is used to deliver a high dose of radiation to a small area in a fairly short period of time.

EXTERNAL BEAM RADIATION THERAPY

Conventional Type

The radiation is delivered through two-dimensional beams using the medical linear accelerator.[6] The aim of stimulation is to accurately target or localize the volume which is to be treated. This technique is well established and is generally quick and reliable. Linear accelerator: High energy radiation is delivered to tumor by this mean.

THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY

Conformal radiation therapy is a geometric shaping of the radiation beam but conforms with the beam's eye view of the tumor. It utilizes the outlining capabilities of the computed tomography stimulator. An enhancement of virtual stimulation in which the profile of each radiation beam is shaped to fit the profile of the target from the beam's eye view using a multileaf collimator. When the treatment volume conforms to the shape of the tumor, the relative toxicity of radiation to the surrounding normal tissues is reduced thereby enhancing a higher dose of radiation to be delivered to the tumor under conventional techniques.[7]

INTENSITY MODULATED RADIATION THERAPY

It is an advanced type of high precision radiation that is the next generation of three-dimensional (3D) conformal radiation therapy.[8] Intensity-modulated radiation therapy (IMRT) improves the ability to conform the treatment volume to the tumor shape, especially when the tumor target is not well separated from the normal tissue. A uniform dose distribution can be created around the tumor by either modulating the intensity of the beam during its journey through the linear accelerator or using multi-leaf collimator.[9] The clinical use of IMRT has grown as computer power increases and cost declines in treating complicated body sites such as central nervous system, head, neck, prostrate, breast, and lung. IMRT is limited by its need for additional time required for operation by experienced medical personal.

STEREO TACTIC RADIATION

Stereotactic radiation is a 3D technique that delivers the radiation in one fraction focusing on the well-defined tumor using extremely detailed imaging scans.[4,10] It delivers the right amount of radiation to the tumor in a short amount of time. There are two types of stereotactic radiations:

Stereotactic radiosurgery and stereo tactics body radiation therapy.

Brachytherapy

Brachytherapy is a term used to describe radiation treatment in which the radiation source is in contact or placed next to the area of the targeted tumor.[11] Brachytherapy is commonly used as an effective treatment for cervical, prostrate, breast, and skin cancer. The dose distribution is almost totally dependent on the inverse square law because the source is usually within the tumor volume. Due to the inverse square law dependence, proper placement of the radiation source is crucial. This means the irradiation only affects a very localized area. These characteristics of brachytherapy provide an advantage over external beam radiation therapy by reducing the probability of unnecessary damage to the surrounding healthy tissue.[4] Brachytherapy procedures can be performed with either temporary or permanent implants.

Temporary Implant

Temporary implants can be high dose rate or low dose rate and usually have long half-life than permanent implants. For high dose rate, the radiation source is put into the place for a few minutes at a time and then removed. This process may be repeated depending on the treatment plan. For low dose rate the radiation source stays up in the target place for up to 7 days. Care should be taken to prevent the implant from moving.

Permanent Implant

These are put right into the tumor using thin hollow needles, once placed these sources give off radiation for several weeks or months.

The temporary and the permanent sources can be manufactured in several forms such as needles, seeds, pellets, ribbons, and tubes. All temporary sources are inserted into catheters that are placed in the tumor during surgery.[4,11]

INTRAOPERATIVE RADIATION THERAPY

This technique is used during surgery. The radiation may be given using a machine for external beam radiation (linear accelerator) or using radioactive substance or placing radioactive substance into the treatment area for a short time (like brachy therapy) during a surgery. Intraoperative radiotherapy is a useful method for treating tumors that are deep inside the body, as the normal tissue is moved aside during surgery exposing the target area. One large dose of radiation is directed straight at the target region after much of the tumor is possibly removed without going to normal tissue. Shielding of the normal tissue can also be done for further protection.[12,13]

Radio Isotope

Systemic radioisotope therapy is a form of targeted therapy. Targeting can be due to the chemical properties of the isotope such as radioiodine which is specifically absorbed by the thyroid gland a thousand-fold better than other bodily organs. Targeting can also be achieved by attaching the radioisotope to another molecule or antibody to guide it to the target tissue. The radioisotopes are delivered through infusion (into the bloodstream) or ingestion.[14]

Commonly used radioisotopes are as follows:

Route of delivery	Radio-isotope	Target cell
Infusion	Metaiodobenzylguanidine	Neuroblastoma
Oral	Iodine - 131[15]	Thyroid cancer or thyrotoxicosis
Hormone bound	Lutetium - 177	Neuroendocrine tumors
Hormone bound or injection	Yttrium - 90	Neuroendocrine tumors, liver tumors.
External beam radiation	Strontium - 89[16]	Bone metastatis and prostrate cancer
External beam radiation	Samarium - 153 lexidronam[17]	Bone metastatis and prostrate cancer

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