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Radiation Therapy for Cancer Treatment

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ABSTRACT

Cancer is one of the most feared and devastating diseases affecting mankind. Radiation is recognized as one of the agents causing cancer via a complex and multi-step process. Radiation Therapy is a highly effective, non-invasive and well established treatment for many types of cancers. The three different methods by which radiation is delivered are External Beam Radiation, Internal Radiation (Brachytherapy) and Systemic Radiation. The choice of therapy depends on the type, stage, location, size of the tumor and the general health of the patient. All these modes of therapy are the primary mechanisms that seek to kill cancer cells by destroying their cell DNA. Radiation Therapy offers several benefits pertaining to cancer treatment; it shrinks or destroys tumors before and after surgery while minimizing damage to nearby healthy tissue. It alleviates symptoms, improves quality of life, while reducing metastasis, recurrence and early stage cancer. Although Radiation Therapy has saved thousands of lives, it is not free from stigma. Some side effects of Radiation Therapy are nausea, fatigue, and vomiting. It may be used in non-cancerous conditions such as benign tumors as well. Although great progress has been made in Radiation Therapy, there is still room for improvement. Radiation Therapy is most effective when combined with Surgery, Chemotherapy and Immunotherapy. Additionally, a new school of thought has emerged in the use of Antioxidants during and after Radiation Therapy. Most recently, a focus on the bi-modal approach of using Radiation Therapy and Immunotherapy to treat cancer is now at the forefront.

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Introduction

The world wide incidence of cancer is a major public health concern and it is a global threat [1, 2, 6]. Cancer is the second leading cause of death in the Western World and the leading cause of death, globally [6, 7]. It is one of the most feared and devastating diseases affecting mankind. The word cancer is synonymous with death and despair. It is indiscriminate in nature as it affects all people - young and old, men and women, adults and children alike. The American Cancer Society projected approximately 20 million newly diagnosed cases and 9.7 million deaths attributed to cancer in 2022 [4, 5]. It is said by 2050, 35 million cases are to be expected. If this current trend continues, cancer has the potential of becoming the world's biggest killer [1]. Despite billions of dollars being spent on cancer research over the years, the death rates from cancer are actually increasing and a cure seems elusive [6,7].

The body is composed of billions of cells. All cells in the body undergo a cycle of growth, division, death and rebirth. Occasionally some cells do not follow the normal life cycle pattern - they divide faster, display unregulated growth and do not die. With time, the uncontrolled growth and accumulation of these cells form a cancerous immortal malignant mass which in turn invades and metastasizes to other organs and different parts of the body. Cancer can occur almost anywhere in the body. The most common types of cancer are breast, prostate, lung and pancreas [2, 8-11].

Chemicals, radiation and viruses have been recognised as cancer causing agents in humans. Although there is a great diversity in the nature of these agents, the end cellular response is always the same - the production of cancer. Initially these agents react with cell DNA (genetic material of cells) and cause damage or alterations to the cell. These damaged or altered cells progress to form preneoplastic cells which finally develop into malignant or cancerous cells [12, 13].

The transformation from normal to cancerous cells is a complex and multi-step process including initiation, promotion and progression. There are more than 100 different types of cancers with multifactorial etiologies that are clinically distinct with cellular and molecular abnormalities. Because of this, finding a unique and unified cure is very difficult [6, 7, 15].

To better navigate this transformative process, Hanahan and Weinberg published a groundbreaking paper outlining 6 hallmarks of cancer: 1. Sustaining proliferative signaling, 2. Evading growth suppressors, 3. Environmental independence for growth, 4. Inducting angiogenesis, 5. Evasion of apoptosis, 6. Invasion and metastasis to different parts of the body [15,16].

Furthermore, most cancers are often diagnosed at the late stage when metastasis has already occurred by traveling through the blood or lymphatic system to most parts of the body such as the bones or liver [2, 8].

The most predominant type of cancer in women is breast cancer and in men, prostate cancer. In both genders, the most common cancers are colorectal and lung cancers. In addition to these, there are other types of cancers which include melanoma, hepato-cellular carcinoma, bladder, leukemia, lymphoma and multiple myeloma. Still significant, but less common are ovarian, testicular

and multiple myeloma. Pancreatic, brain and uterine carcinomas are the most fatal of cancers; although they are not among the most common cancers. One in two men and one in three women are expected to develop cancer over their lifetime. New breakthroughs in diagnosis, detection and treatment have markedly improved survival rates, but, we are still a long way away from a definitive solution [6, 7, 14].

The most frequently used method in the treatment of cancer is Radiation Therapy (RT). RT offers a safe, very effective, highly precise, non-invasive, targeted and versatile method which is used for the majority of cancer types. Its other benefits are improved survival rates, palliative considerations, mitigating side effects and most importantly, preserving quality of life.

Approximately half of all cancer cases make use of RT. The purpose of this paper is to bring a concise overview on RT.

Radiation Therapy in Cancer Treatment

Surgery, chemotherapy and radiation are the main treatment protocols for cancer cases [2, 8]. The choice of therapeutic strategy depends on the type and stage of cancer. All these therapeutic strategies have been found to be effective in reducing tumor mass. However, today more than half of the patients diagnosed with cancer receive RT. RT is commonly used for cancer patients as it is safe and effective for just about every type of case. RT contributes to the treatment of nearly 40% of treatment plans [14, 18-24]. RT shrinks or destroys tumors, diminishes symptoms and improves quality of life while minimizing damage to the surrounding tissue. Other names for RT are x-ray therapy, radiotherapy or irradiation. RT uses high energy particles or waves such as electron beams, x-rays, gamma-rays or a proton beam to destroy or damage cancer cells [18].

At lower doses RT is used to examine dental and bone structures in the buccal cavity by dentists (45); or to examine abnormalities in bone-related disease by radiologists [25, 26].

At high doses, RT kills cancer cells by two different mechanisms - directly and indirectly [27-29].

Direct Mechanism

Cell DNA is the control mechanism for how cells grow, divide and repair themselves. In direct mechanisms, RT damages cell DNA beyond repair by stopping cells from dividing. During this process healthy cells are also damaged along with cancer cells. However, healthy cells can repair themselves at a much faster rate than cancer cells. The goal of RT is to damage cancer cells, while sparing as many healthy cells as possible [28-32].

Indirect Mechanism

For the Indirect mechanism, RT kills cancer cells by ionizing water molecules in the cytoplasm, generating free radicals (FR) or reactive oxygen species (ROS). It is the FR and ROS that damage cell DNA, which in turn leads to cell death [33].

In both mechanisms, DNA is damaged beyond repair. RT does not kill cancer cells right away, it takes days or weeks of treatment before DNA is damaged - the cancer cells keep dying for weeks and months after RT ends. When the damaged cells die, they are broken down and removed from the body. Besides indirect and direct mechanisms for eradicating cancer cells, other natural mechanisms include necrosis, apoptosis, autophagy and mitotic cell division are also affected by radiation.

Radiation Necrosis (RN)

RT is highly effective at targeting cancer cells. In rare cases it can damage normal tissue. RN or osteoradionecrosis is often encountered by pathologists examining biopsy material as a delayed phenomenon many months or years after radiation is administered. It may occur in 5-37% of patients. RN has potentially fatal complications after RT treatment. RN makes it hard for the body to build new tissue, fight infection or heal skin [30-32].

Apoptosis

Apoptosis is often induced after radiation. The initiation of apoptosis is mainly activated by two different pathways - intrinsic and extrinsic; both of which ultimately complete apoptosis by activating the extrinsic pathway. Additional RT can promote apoptosis in other pathways such as P53 and SAPK/JNK. This damage is now thought to be stabilized by telomere capture, which is a transfer of telomeres from normal chromosomes to broken chromosomes [28-32].

Autophagy

It is known that RT is one of the stressors that induce autophagy in both normal and cancer cells. Autophagy has been shown to play a dual role with evidence for both cytoprotective and/or cytotoxic effects; depending on the heterogeneity of each tumor. Studies have suggested that autophagy suppresses tumor growth in the early stages, but accelerates tumor progression in the later stages. Hypoxia plays an important role in induced RT and is responsible for many molecular changes within the cell. Understanding the relationship between RT, hypoxia and autophagy is crucial [30-32].

Mitotic Cell Death or Mitotic Catastrophe

After RT most solid tumor cells are formed mainly as a result of aberrant mitotic events causing missegregation of chromosomes which then form giant cells with multiple nuclei with abnormal nuclear morphology [28-32].

Senescence

This occurs in cancer cells through extensive RT treatment causing severe damage to cell DNA and finally death due to apoptosis [29, 32-34].

How Radiation Therapy is Given

RT uses high energy waves to destroy or damage cancer cells. It is given in three different ways depending on several factors: the type of cancer, size of cancer, location of cancer, stage of cancer and the general health of the patient. The three delivery methods are [35-36].

External Beam Radiation Therapy (EBRT): EBRT is the most frequent type of treatment for cancer. In this approach a machine called a Linear Accelerator directs high energy rays from outside the body to a carefully targeted mass within the body. It is done at hospitals or RT treatment centers. The patient usually lies on a table and radiation is targeted at the tumor site from different angles. It is given usually on an outpatient basis over a period of several weeks at varying frequencies. EBRT is used to treat breast cancer, lung cancer, prostate cancer, colon cancer and cancers of the head and neck [37, 38].

Internal Radiation Therapy (IRT): IRT also known as Brachytherpy. In this treatment, a radioactive source or implant is put inside the body directly or very close to the tumor. The implants come in different forms or shapes which include tube, wire, capsule/seeds/pellets (caesium, iridium or cobalt). This allows higher doses of

radiation to be delivered to the tumor while reducing exposure to the healthy cells. It is commonly used for prostate, cervical and breast cancers amongst others. The implant in the body may be placed for a shorter period such as 10-20 minutes and the treatment is repeated periodically. Once the course is complete the implant may be removed or sometimes the implant (iodine-125) remains in the body permanently until the treatment is stopped [32-35].

EBRT and IRT have one thing in common: both are local treatments that work on one part of the body by directing high energy beams at cancer cells. However, the two differ in the source of radiation. In EBRT the radiation is delivered from a machine outside of the body while in IRT, the radiation is delivered from an implant.

Systemic Radiation Therapy (SRT)

This type of therapy uses radioactive drugs called radiopharmaceuticals or radionuclides (technetium-99m, iodine-131). Radioisotopes are linked to monoclonal antibodies that are easily detected and targeted for destruction. Some monoclonal antibodies trigger an immune system response that destroys the outer membrane of the cancer cell thereby blocking cell growth. SRT is delivered orally or through IV and travels through the bloodstream to target and kill cancer cells. SRT affects the whole body which means body fluids such as urine, sweat and saliva will give off radiation for a while. SRT is used to treat certain types of cancers including thyroid, bone and prostate cancer [39-42].

Radiation Therapy Professionals

During radiation therapy, a team of trained medical professionals administer the treatment protocol. The team includes one or many of the following [43, 44].

Radiation Oncologist: This doctor is specially trained to treat cancer with radiation. This medical professional oversees the radiation treatment plan.

Radiation Physicist: This medical professional is involved in ensuring the radiation equipment is working and delivers the exact dose prescribed by the Radiation Oncologist.

Dosimetrist: This medical professional assists in planning the treatment.

Radiation Therapist: This medical professional positions the patient and operates the Linear Accelerator to deliver treatment.

Radiation Therapy Nurse: This medical professional assists with managing side effects of RT.

Radiation Therapy in Non-Cancerous Disease

RT is often used in the treatment of cancer - but at times it can also be used in some non-cancerous situations. These special conditions include [45-49].

Benign Tumors: Such as acoustic neuromas and pituitary adenoma non-cancerous.
Blood Disease: Such as polycythemia vera and mycosis.
Inflammatory Conditions: Such as Dupuytrens and keloids.
Thyroid Conditions: Use of radioactive iodine for certain thyroid disorders.
Vascular Conditions: Arteriovenous disorders and to prevent the re-narrowing of blood vessels
Eye Conditions: Eye diseases such as macular degeneration and uveitis.
Hypertrophic Scarring: To prevent the recurrence of hypertrophic scars or keloids.
Autoimmune Disease: Used for disorders like rheumatoid arthritis, scleroderma and lupus.
Gynecologic Conditions: Used for conditions such as endometriosis and excess bleeding from uterine fibroids.
Dental Conditions: Used to treat certain conditions in teeth and oral cavity.

Beneficial Effects of Radiation Therapy

RT is a popular and effective treatment option in battling cancer. Some of the more salient features of RT are described as follows. RT is Non-Invasive in nature. It offers the potential for a cure without the need for incisions or unnecessary risks that come from surgery. It reduces surgical complications and offers better recovery times [50-52].

Modern advances in RT offer treatment plans which are highly targeted. Modern RT techniques such as image-guided radiation therapy (IGRT), stereotactic radiosurgery (SRS) and intensity-modulated radiation therapy (IMRT); all deliver doses of radiation with an exacting accuracy and intensity all while minimizing damage to surrounding healthy tissue. This is particularly beneficial for cancers that have not metastasized or for managing metastatic symptoms.

Another salient feature of RT is that it provides the greatest versatility in treatment plans. RT can be used to treat various types of cancers such as breast, prostate, brain and lung to name a few. Additionally, with modulated doses, it also allows for the treatment for non-cancerous conditions such as benign tumors.

Most importantly, RT offers the best Quality of Life benefits as compared to other treatment options. With chemotherapy and surgery, quality of life considerations such as lingering toxicity, longer surgical recovery times and poor pain management options are all minimized. The highly targeted and precision controlled nature of RT gives the best possible outcome by impacting cancer cells while preserving healthy tissue. This rings true more so for advanced cases where a cure is not possible.

The Cost Effective nature of RT is demonstrated in its delivery and the pre/post activities surrounding treatment plans. In several cases, RT is administered on an outpatient basis, allowing patients to return home and resume normal daily activities without needing extensive post-treatment hospital care.

In certain cases, RT combined with other treatment options (Surgery and/or Chemotherapy) are required to increase the overall effectiveness of the treatment plan. This combined approach is often more successful in treating certain types of cancer.

Side Effects of Radiation Therapy

While RT is highly effective in treating cancer, it can also cause unwanted side effects. These side effects vary depending on factors such as the radiation dose, delivery location, general health of the patient and the duration of treatment. Most side effects subside or disappear after the treatment ends. Some of the more notable side effects are [23,51,53-59].

Fatigue: Many patients experience fatigue during RT, which ranges from mild to severe. This fatigue may persist for weeks or months after the completion of treatment.

Nausea and Vomiting: One of the more common side effects of RT is nausea and vomiting. RT delivered to areas of the body such as the abdomen or pelvis cause these symptoms. These however can be corrected through medication.

Hair Loss - RT delivered to the head or neck can cause hair loss in the treated area. Hair typically grows back after treatment, but may have a different texture or appear to be thinner.

Bone Marrow Suppression: RT can affect the production of blood cells. Low blood cell counts (RBC, WBC and platelets) can increase the risk of infection, anemia, internal bleeding and fatigue.

Difficulty Swallowing: RT to the head and neck area can cause inflammation and narrowing of the esophagus, leading to difficulty in swallowing. These symptoms may require dietary changes or additional treatment.

Skin Changes: RT can cause skin irritations such as redness, itching, dryness and peeling over the treated area. These symptoms are very similar in nature to a sunburn. It usually goes away after the treatment ends.

Lymphoedema or Swelling: RT can cause lymphatic or immune system responses causing lymphoedema or swelling (edema) in the treated area. This holds especially true if it is near a major organ or lymph node. It is most commonly found in the arms or legs, but can also affect other parts of the body. Swelling usually subsides over time but may require medical intervention.

Changes in Taste or Appetite: Another common side effect of RT is the loss of appetite or change in taste perception. These effects are temporary and should be managed by a nutritional dietary intake.

Long-Term Effects: Some long term side effects of RT may include fibrosis (scarring) of the treated area and more alarmingly it can lead to secondary cancers. The risk of developing secondary cancers is higher in older patients [60].

Emotional and Psychological Effects: A cancer diagnosis in general will undoubtedly cause anxiety, emotional distress and depression. Supportive services through the American Cancer Society, private counseling, support groups, family and friends can all help manage the process.

Lung irritation: RT delivered to the chest can lead to coughing, shortness of breath and lung inflammation (pneumonitis).

Fertility Issues: RT to the pelvic region can affect reproductive organs, potentially leading to infertility and other complications.

Other Limitations of RT: RT is less effective when dealing with larger tumor masses or tumor masses where a poor blood supply exists (i.e. angiogenesis). For smaller tumor masses, RT gives way to SRT.

Cancer patients and their care teams can assist with various side effects through medication, lifestyle modification and social support care to improve quality of life during and after treatment.

The Benefits of Combining Radiation Therapy and Surgery

Focusing on the goal of improving survival rates, at times a more tailored approach to cancer treatment is needed. Combining RT with surgery offers several benefits that each treatment protocol alone cannot offer. Parameters such as tumor size, location, stage as well as the patient's general health will play into the treatment planning process. A few salient benefits are [61].

Tumor Mass Reduction: RT before or after surgery (adjuvant therapy) can either shrink tumors making them easier to remove or targeting remaining cancer cells after surgery (i.e. micrometastases). The goal is to reduce the risk of cancer recurrence.

Local Control: Controlling cancer growth locally through RT with surgery increases the chances that cancers with a high risk of local recurrence remain in check.

Tissue/Organ Preservation: In certain cases combining RT with surgery may allow for tissue/organ preservation. Sphincter saving surgery instead of a permanent colostomy may be realized through neoadjuvant RT.

Reduced Metastasis: RT along with surgery may reduce the risk of metastasis by eliminating or reducing the mass of the tumor.

Risk of Recurrence: RT along with surgery may assist in reducing cancer recurrence rates. This especially holds true for cancers with aggressive or high-risk profiles.

Side Effects of Combining Radiation Therapy and Surgery

The goal of delivering the best potential patient outcomes can be enhanced by combining RT with surgery - but this does not come without certain risks. Certain side effects are more prevalent when both treatment modalities are combined. These side effects are dependent on underlying factors such as the type and location of cancer, the extent of surgery and the dosage and duration of RT. A few risks and side effects are noted:

Tissue Damage and Wound Healing: Combining RT with surgery may increase the risk of tissue damage and wound healing complications. Tissue damage and wound healing complications are evidenced by delayed healing, tissue necrosis, impaired tissue function, infections, dehiscence (wound opening) and seromas (fluid collections). The risk of tissue fibrosis and scarring result in stiffness, reduced flexibility and functional impairment of tissue or organs.

Stressors and Delayed Recovery: A direct result of tissue damage and wound complication using adjuvant therapies can manifest itself by increased fatigue, overall patient discomfort, the possibility of additional medical intervention and prolonged healing/recovery times.

Sensory Changes: RT combined with surgery may lead to sensory changes such as numbness, tingling, lymphedema or hypersensitivity in the treated area. These sensory changes have the potential to persist long after treatment and can impact daily activities and quality of life considerations. These side effects may be characterized as chronic and will most likely require medical intervention or require ongoing management.

Secondary Cancers: When treating cancer with RT alone or with adjuvant therapies, the risk of developing secondary cancers at the treatment site is elevated - this is especially true for elderly patients.

Gastrointestinal and Urogenital: Cancers that appear in the lower abdomen or pelvis such as colorectal or gynecological - RT combined with surgery can lead to side effects and complications like diarrhea, urinary frequency, and sexual dysfunction.

Skeletal and Bone Health: Bone health considerations such as osteoporosis, fractures and bone necrosis may be impacted by RT combined with surgery.

Combination of RT and Chemotherapy

Chemoradiation or concurrent chemoradiotherapy is a common treatment protocol offered in many cancer cases [62-66, 67]. This approach uses RT and chemotherapy in conjunction with each other. Similar to any adjuvant approach, these two treatment modalities used in conjunction offer a highly personalized treatment plan tailored to the patient's disease profile per the tumor size, tumor location, tumor stage and patient health. This multidisciplinary approach maximizes treatment efficacy. Some key aspects are:

Tumor Control & Synergistic Effect: The use of chemotherapy sensitizes cancer cells to RT thereby making them more susceptible to its damaging effects. This is an excellent example of how the multimodal use of RT and chemotherapy displays a synergistic effect and greater tumor control.

Tumor Size and Metastasis: RT can shrink tumor size. Any microscopic cancer cells that have spread beyond the primary tumor site can be addressed by chemotherapy. This is yet another use case of how adjuvant therapies can better control the risk of local recurrence, distant metastases (i.e. systemic) and improve overall treatment efficacy.

Improved Survival Rates: A multimodal approach using both RT and chemotherapy can lead to improved patient survival rates for certain types of cancers - specifically, locally advanced or aggressive ones.

Organ Preservation: Chemoradiation can better assist with organ preservation when a reduction of the tumor mass near organs where function and integrity are of paramount concerns (i.e. rectal cancer).

Side Effects of Combining Radiation Therapy and Chemotherapy

Another adjuvant protocol in treating cancer is the use of RT and chemotherapy. Although effective, it too has its share of side effects. A patient's healthcare team will provide the appropriate monitoring and management of side effects such that quality of life parameters are preserved [68].

Increased Toxicity: The cumulative effects of employing both modalities may lead to more pronounced side effects. These side effects can include nausea, vomiting, fatigue and hematologic toxicity. Hematologic toxicity suppresses bone marrow function leading to a decreased production of RBC and WBC. Low RBC increases the risk for anemia. A low WBC increases the risk for thrombocytopenia (low platelet count) which in turn results in more infections, bleeding and fatigue.

Sensory Changes: The combination of RT and chemotherapy can lead to sensory changes such as mucositis, esophagitis, skin reaction and gastrointestinal side effects. The symptoms of each sensory change can be described by the following respectively - inflammation and damage to the lining of the mouth, throat and esophagus which affects swallowing, eating and overall nutritional intake; skin reactions such as redness, itching, dryness and peeling; diarrhea, abdominal pain and bowel dysfunction. Each of these symptoms may dissipate after the treatment ends or may require ongoing medical intervention and care management.

Long-Term Side Effects: The combination of this multimodal treatment protocol is not dissimilar to any other singular or combined treatment protocol. Close monitoring and follow up care are essential in the management of quality of life considerations (i.e. physical, emotional and psychological).

Combination of Radiation Therapy and Immunotherapy

Combining RT with immunotherapy is a very promising approach in cancer treatment. Some potential benefits of combining these two modalities [69-77].

Tumor Response Synergies: Immunotherapy works by amplifying the body's immune response to recognize and attack cancer cells. RT creates an immunogenic tumor microenvironment, making cancer cells more susceptible to immunotherapy-induced activation. Together these two treatment modalities create a formidable treatment synergy offering.

Growth and Metastases Control: Immunotherapy has the potential to target distant metastases that may not be directly accessible by RT. The combination of both can result in a systemic immune response leading to the regression of both primary tumors and metastatic lesions; thereby suppressing tumor recurrence.

Immune Memory and Abscopal Effect: Immunological memory is a phenomenon where the immune system remembers or recognizes cancer cells even after treatment. The abscopal effect refers to a rare phenomenon where localized RT results in the regression of distant untreated tumors. It appears that a recognition system or identification system is activated through immunotherapy. Given in conjunction with RT a highly efficacious treatment can be realized with long-term protection against cancer recurrence.

Radioresistant Tumors: In certain cases, tumors have been known to show limited or no response when RT is administered alone. Immunotherapy has demonstrated its ability to activate immune cells to target and kill radioresistant cancer cells. Once again the potential for highly efficacious treatments are available with this multimodal approach.

Side Effects of Combining Radiation Therapy and Immunotherapy

While the combination of RT and immunotherapy holds great promise, side effects are known to exist due to the complexities of the immune system and radiation damage. In this bimodal treatment, the immune system is activated against normal tissue. This leads to complications such as dermatitis, colitis, pneumonitis, thyroiditis, hepatitis, and endocrinopathies [78,79].

Radiation-Induced Toxicities: RT can cause acute and late stage toxicities in and around the treated tissue. When combined with immunotherapy, these toxicities increase inflammation and immune activation at the radiated site.

Radiation Dermatitis: Skin irritation, redness, itching and peeling of the treated area is a result of combining RT with immunotherapy. Radiation dermatitis may be more severe and prolonged due to increased immune activity in the skin.

Gastrointestinal Toxicities: Both RT and immunotherapy can cause gastrointestinal toxicities resulting in diarrhea, abdominal pain and colitis. These are usually severe and difficult to manage leading to dehydration and electrolyte imbalances.

Pulmonary Toxicities: RT when combined with immunotherapy, increases the risk of pneumonitis due to immune mediated lung inflammation.

Hematologic Toxicities: When combined with RT, immunotherapy can suppress bone marrow function, leading to hematologic toxicities such as neutropenia, thrombocytopenia and anemia.

Wound Healing: RT when combined with immunotherapy can cause inflammation and immune activation. This results in impaired wound healing and skin ulcers at the irradiated tissue.

Neurologic Toxicities: RT when combined with immunotherapy increases the risk of neurologic toxicities due to immune-mediated inflammation in the central nervous system. This can cause cognitive impairment, radiation necrosis and radiation-induced neuropathy.

Endocrine Dysfunction: RT when combined with immunotherapy increases the risk of endocrine toxicities including thyroid dysfunction, adrenal insufficiency and hypophysitis. This can cause hormonal imbalances and endocrine dysfunction.

Alternative Treatments to Radiation Therapy

Many cancer patients are fearful and experience adverse side effects of RT - not surprisingly, 80% of them look for alternate treatments. As a result, many cancer patients are now turning to dietary supplements (DS) or nutritional supplements (NS) to improve their prognosis, quality of life, energy levels, appetite, nausea control and enhanced immune systems.

There is a common perception that the taking of antioxidant supplements can decrease the effectiveness of RT on cancer cells, as antioxidants protect cancer cells against damage [79-83].

There are many expert opinions that believe scientific evidence does not support the use of antioxidants during cancer therapy . This is due to the belief that antioxidants can both interfere with treatment and protect healthy cells.

One group of medical practitioners support and recommend the use of antioxidant supplements during radiation. DS/AO protects against radiation by producing beneficial results such as decreased toxicity and fewer side-effects. There are however, many studies that show that antioxidants play a dual role in healthy and cancer cells: they protect healthy cells against damage and at the same time, these nutrients exhibit a pro-oxidant action in damaged cells that accelerates cellular death from radiation [80-82].

The opposing view states that taking antioxidant supplements during cancer treatment is harmful due to its potential interference in RT and chemotherapy. RT works by generating free radicals causing oxidative damage; the subsequent build up of oxidative stress in turn reduces the efficacy of treatment. Antioxidants help keep free radicals from causing oxidative damage. Antioxidants scavenge or neutralize free radicals that may protect tumor cells and potentially interfere with the treatment's ability to destroy cancer cells. For this reason, it is recommended that patients avoid antioxidant supplements until the completion of RT, then resume taking antioxidant supplements [81-83]. Both these groups have strong opinions on their views based on prevailing opinion rather than clinical evidence regarding the risk/benefit profile of taking antioxidants. Discouraging patients from using these beneficial antioxidants during radiation treatment is detrimental to their recovery and health.

During Radiation Therapy

During RT Treatment, patients should follow all guidelines outlined by their treatment team. Some examples are [84-86].

Treatment Schedule: Consistency in treatment is paramount for its effectiveness and as such patients are to attend all scheduled radiation therapy sessions.

RT Treatment Session: RT treatment will require proper positioning and the use of shields and other protective devices to minimize radiation exposure to healthy tissue. Follow all directions carefully to achieve the maximum benefit.

Skin Care: RT is typically very hard on the skin and its effects range from mild irritation to more severe side effects like redness, itching, and peeling. A proper skin care regime which includes the use of mild, fragrance-free soap and lukewarm water to wash the treated area and using fragrance & alcohol free moisturizers to keep the skin hydrated and healthy. Avoid exposing treated areas of the skin to sun exposure - especially during the hours of 10-4 where the sun's rays are typically the strongest. Wear loose fitting, non-restrictive, protective clothing such as hats and long sleeves and use Sun Protective Factor 30 or higher to block the harmful rays of the sun. Also, avoid rubbing and scratching the skin.

Fluids & Nutrition: Good nutritional intake coupled with plenty of fluids promotes a boost in immunity, keeps the body strong and minimizes side effects such as fatigue.

After Radiation Therapy

At the end of RT Treatment, patients typically go through a phase of post-treatment follow-up and recovery. Some examples are [84-86].

Post RT Appointments: Patients receive regular follow up appointments with their radiation oncologist to monitor progress, evaluate treatment response and monitor for tumor recurrence. These follow on activities may include physical exams, imaging (i.e. CT or MRI) and laboratory tests (blood work, organ functions, etc.) to assess cancer status.

Monitoring and Managing Side Effects: Patients often experience side effects during and after RT treatment. Symptoms include fatigue, skin irritation, hair loss, nausea, pain, swelling, difficulty swallowing or any functional changes to the bowels or bladder. Pay close attention to any changes and seek the advice of healthcare providers who will assist in maintaining quality of life considerations.

Long Term Complications: Long term complications may develop months or years after treatment. Some of these long term complications include radiation-induced fibrosis, nerve damage, impaired organ function and secondary cancers. Healthcare providers will recommend appropriate medical intervention as needed.

Recovery and Rehabilitation: Depending on the type of cancer, radiation intensity, duration of treatment, intensity of potential side effects, patient recovery and rehabilitation times will vary from case to case. Regular exercise will help maintain strength, flexibility, and cardiovascular health. A good nutritional diet will support healing and overall health. Smoking cessation will reduce the risk of complications. Alcohol avoidance will help the body's ability to heal and decrease the risk of side effects. All these factors help in the recovery process.

Psychological & Emotional Support: RT can be an extremely physically and emotionally challenging event. Many patients experience anxiety, depression and other psychologically or emotionally charged feelings. Healthcare providers will assist by providing counseling and introduction to support groups to help navigate these challenges. Stress reducing activities such as meditation, deep breathing and yoga also all promote relaxation and emotional well-being.

Getting Back to Normal: After RT and the effects of any treatment complications subside, patients can gradually resume their normal duties and daily routines. It is important to seek the advice from healthcare professionals about dietary guidelines, medications, safely returning to work, exercising or activity restrictions.

Advances in Radiation Therapy

In recent years several significant advances in RT techniques, improving its effectiveness, reducing side effects and expanding its applications. Some advances in RT techniques such as 3D Conformal RT, stereotactic body radiation therapy (SBRT), proton therapy, intensity-modulated radiation therapy (IMRT), Image guided RT all enable precise delivery of high doses of radiation to tumors while sparing surrounding healthy tissue [87-90].

3D Conformal RT: Uses CT scans and computer software to create 3D models of the tumor. Using these models as a guide, the machine directs radiation beams that target the cancer site while sparing healthy tissue. Several cancer types have seen improved outcomes from this including brain cancer, head and neck, liver cancer lung cancer and prostate cancer.

Stereotactic Radiation Therapy (SRT) and Stereotactic Radiosurgery (SRS): These techniques deliver very high doses of radiation with extreme precision in typically one to five sessions. They are particularly effective for small tumors in the brain, spine, lung, liver and other areas. They offer excellent tumor control while sparing surrounding healthy tissue.

Intensity-Modulated Radiation Therapy (IMRT): IMRT allows for more precise targeting of the radiation beam to conform to the shape of the tumor while minimizing exposure to surrounding healthy tissue. This technique is especially useful for tumors located near critical organs or structures.

Image-Guided Radiation Therapy (IGRT): IGRT uses advanced imaging techniques such as CT scans or MRI to precisely locate the tumor immediately before each treatment session. This ensures accurate delivery of radiation even if the tumor or surrounding anatomy shifts slightly between sessions.

Proton Therapy: Proton therapy delivers radiation using protons instead of traditional X-rays. Protons deposit their energy more precisely thereby reducing radiation exposure to nearby healthy tissue. This makes proton therapy particularly advantageous for treating tumors near critical structures or in pediatric patients.

Particle Therapy: In addition to proton therapy, other forms of particle therapy such as carbon-ion therapy are being explored. These therapies offer the potential for even greater precision and effectiveness in targeting certain types of tumors, particularly those that are resistant to traditional RT.

Radiomics and Radiogenomics: These emerging fields use advanced imaging techniques and computational analysis to extract quantitative data from medical images. This information can help predict a tumor's response to RT and assist in treatment planning allowing for a more personalized and effective treatment.

Hypofractionated Radiation Therapy: This approach delivers higher doses of radiation in fewer treatment sessions. It has demonstrated similar results as standard regimens for certain cancers, offering the advantage of shorter treatment sessions and reduced overall treatment time.

Intraoperative RT (IORT): IORT delivers radiation during surgery. After the tumor is removed surgically, IORT destroys any remaining cancer cells.

Immunotherapy and RT Combinations: There is growing interest in combining RT with immunotherapy to enhance the immune system's response to cancer. Radiation can help "prime" the immune system by releasing tumor antigens and altering the tumor microenvironment, potentially improving the effectiveness of immunotherapy.

In addition to the technological advances mentioned above, there are other evolutionary advances that highlight the ongoing developments in RT with a focus on improving outcomes, reducing side effects and expanding its applicability across various cancer types and clinical scenarios.

Conclusions

The goals of RT can vary depending on factors such as the type of cancer, stage of disease, and overall treatment plan. However, the primary objectives of radiation therapy in cancer treatment include [91-92].

Tumor Control: One of the primary goals of RT is to eliminate or eradicate cancer cells within the primary tumor and any adjacent tissue (i.e. preserve organ functions). It also inhibits the ability of the tumor to proliferate or metastasis. Doing this provides relief from symptoms and potential side effects.

Palliative Considerations: In cases where cancer cannot be cured, Palliative RT is used to alleviate pain, symptoms and improve quality of life in cases of advanced or metastatic cancer.

Adjuvant Therapy: RT may be used as adjuvant therapy after surgery or chemotherapy to eradicate residual cancer cells, reduce the risk of local recurrence and improve treatment outcomes. Adjuvant RT is commonly used for cancers with a high risk of recurrence such as breast cancer and head & neck cancers.

Neoadjuvant Therapy: RT may be given as a neoadjuvant therapy before surgery or chemotherapy. The goal is to shrink the tumor with RT thereby making it easier to surgically remove the tumor.

Long-Term Disease Control: Prophylactic RT is used to prevent the recurrence of cancer in high-risk patients or to treat in-situ carcinomas before they progress to invasive cancers. This practice is very relevant to cases pertaining to the breast, head & neck, skin, Hodgkin lymphoma, early-stage prostate cancer.

Overall, the goals of radiation therapy in cancer treatment are tailored to each individual patient's disease characteristics, treatment goals and overall health status. Radiation oncologists work closely with multidisciplinary teams to develop personalized treatment plans that optimize therapeutic benefits while minimizing treatment-related side effects [93-101].

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