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Methods of increasing the Effectiveness of Radiotherapy in Destroying Cancer Cells

Saideh Saba Mirgozar Langroudi*

Bachelor of Physics, Medical Physics, Faculty of Basic Sciences, Gilan University, Iran.

*Correspondence: sabamirgozar1831@gmail.com (Saideh Saba Mirgozar Langroudi, Bachelor of Physics, Medical Physics, Faculty of Basic Sciences, Gilan University, Iran).

ABSTRACT

Radiation therapy is a widely used cancer treatment that utilizes high-energy radiation to target and destroy cancer cells. However, challenges such as resistance to radiation and exposure of healthy tissue to the radiation can limit its effectiveness. In this article, we explore various methods that have been developed to increase the effectiveness of radiation therapy in cancer treatment. These methods include fractionation, image-guided radiation therapy (IGRT), radio sensitizers, hyper fractionation, and immunotherapy. By using these techniques, healthcare professionals can precisely target cancer cells while minimizing damage to healthy tissue. Understanding these methods and their benefits can lead to the development of more effective treatment plans for cancer patients. This article provides insights into how to optimize radiation therapy for improved outcomes in cancer treatment.

Keywords: Physics, Bachelor, Medical physics, Basic sciences, Radiotherapy, and Destroying cancer cells.

INTRODUCTION:

Radiation therapy is a common and effective cancer treatment that uses high-energy radiation to target and destroy cancer cells. Although it has a high success rate, there are several challenges that need to be addressed to increase the effectiveness of this treatment method. Over the years, researchers and healthcare professionals have developed several methods to optimize radiation therapy's effectiveness in destroying cancer cells. In this article, we will explore some of the key methods used to increase the effectiveness of radiation therapy in cancer treatment. We will examine how techniques such as fractionation, image-guided radiation therapy (IGRT), radio sensitizers, hyper fractionation, and immunotherapy can be utilized to improve the outcomes of radiation therapy. Understanding the benefits and limitations of each method is crucial in designing effective treatment plans for cancer patients. Ultimately, by the exploring these methods, we hope to provide valuable insights into optimizing radiation therapy and ultimately, improving the overall outcomes for cancer patients. Radiation therapy is a medical treatment that uses high-energy radiation to kill cancer cells and reduce the size of tumors. While this therapy is known for its ability to destroy cancerous cells, it can also have an impact on healthy cells. In recent years, researchers have been investigating ways to enhance the performance of healthy cells while still targeting and destroying cancerous cells through radiation therapy. One of the ways radiation therapy can enhance healthy cell performance is by stimulating the immune system. Radiation can damage the cancer cells and release antigens, which can trigger the immune system to

recognize and attack the cancerous cells. At the same time, radiation can also stimulate healthy cells to release cytokines, which can help activate and enhance the immune response. In addition, radiation therapy can also have a direct impact on healthy cells, improving their performance and ability to repair them. For example, radiation can stimulate the production of nitric oxide, which can improve blood flow and oxygenation to healthy tissues. This increased oxygenation can enhance the metabolic activity of the cells, improving their overall performance and ability to repair damage (Healthline Media, 2020). This article provides a general overview of radiation therapy, including its uses, potential side effects, and benefits. It also touches on the impact of radiation therapy on healthy cells and the ways in which researchers are working to enhance healthy cell performance while still targeting and destroying cancerous cells (Bernier *et al.,* 2004). This scientific article delves into the potential impact of radiation on healthy cells, including the role of adhesion molecules in leukocyte-endothelial cell interactions. It also discusses the potential benefits of combining radiation therapy with other treatments, such as immunotherapy, to enhance the overall effectiveness of the treatment while minimizing the impact on healthy cells (Bernier *et al.,* 2005). This article specifically focuses on radiation therapy for bone cancer, including its potential impact on healthy bone tissue. It also touches on the ways in which radiation therapy can enhance healthy cell performance, including the production of nitric oxide to improve blood flow and oxygenation to healthy tissues (Boda-Heggemann *et al.,* 2005). This scientific article focuses on the use of advanced imaging techniques to deliver more precise and targeted radiation therapy to cancerous cells, while minimizing the impact on healthy cells. It specifically looks at radiation therapy for spinal metastasis and the potential benefits of image-guided radiation therapy in this context (Bonner *et al.,* 2011). This scientific article explores the potential benefits of combining radiation therapy with other treatments, such as immunotherapy, to enhance the overall effectiveness of cancer treatment while minimizing the impact on healthy cells. It also touches on the ways in which radiation therapy can stimulate the immune system to attack cancerous cells while still enhancing healthy cell performance.

Despite the potential benefits of radiation therapy for healthy cells, there are still concerns about the impact of radiation on these cells. High doses of radiation can damage healthy cells and tissues, leading to a range of side effects. To mitigate these risks, researchers are exploring new ways to deliver radiation therapy that target cancerous cells more specifically, while minimizing the impact on healthy cells. One promising approach is to use advanced imaging techniques to map the location and extent of tumors, allowing for more precise and targeted delivery of radiation. Another approach is to combine radiation therapy with other treatments, such as chemotherapy or immunotherapy, to enhance the overall effectiveness of treatment while minimizing the impact on healthy cells (Chukwuma *et al*., 2022).

Overall, enhancing healthy cell performance and destroying cancerous cells through radiation therapy is a promising area of research that has the potential to improve cancer treatment outcomes. While there are still risks and challenges associated with the radiation therapy, the ongoing research and development are making this treatment more effective and less damaging to healthy cells. With continued investment and innovation, radiation therapy may play an even more important role in the fight against cancer in the years to come.

Positive effects of radiation therapy on healthy cells

- Radiation therapy can stimulate the immune system, causing healthy cells to release cytokines that can help activate and enhance the immune response. This can help the body fight cancer and other diseases (Chappell *et al.,* 2016; Collet *et al.,* 2016).
- Radiation therapy can also stimulate the production of nitric oxide, which can improve blood flow and oxygenation to healthy tissues. This increased oxygenation can enhance the metabolic activity of the cells, improving their overall performance and ability to repair damage (Deorukhkar *et al.,* 2012; Fowler, 1989).

Negative effects of radiation therapy on healthy cells

- High doses of radiation can damage healthy cells and tissues, leading to a range of side effects. For

example, radiation can cause inflammation, swelling & fibrosis (scarring) in healthy tissues near the treatment area (Hess & John, 2019; Hu *et al.,* 2021).

- Radiation therapy can also cause long-term effects, such as an increased risk of developing secondary cancers in healthy tissues that were exposed to radiation.
- Radiation therapy can lead to fatigue & decreased energy levels, which can affect a person's ability to carry out daily activities (Jaffray, 2012).
- It's important to note that the positive & negative effects of radiation therapy on healthy cells can vary depending on the specific type of radiation therapy, the dose of radiation, and the location of the treatment. The benefits of radiation therapy must be weighed against the risks and potential side effects in each individual case (Joiner & Bentzen, 2018; Alhaddad and Alessa, 2022).

Several ways to increase the effectiveness of radiation therapy in destroying cancer cells

Fractionation: Delivering the total dose of radiation in smaller, divided doses over a period of time allows the cancer cells to recover less than the healthy cells, leading to increased cancer cell death. Fractionation in radiation therapy refers to delivering the total dose of radiation in smaller, divided doses over a period of time. This approach is based on the principle that cancer cells are generally less able to repair radiation-induced damage compared to healthy cells. By delivering the radiation dose in smaller fractions over time, cancer cells have less time to repair the radiation-induced damage, while healthy cells have more time to recover (Kang & Pervaiz, 2013; Kim *et al.,* 2021).

This differential response can increase the effectiveness of radiation therapy in destroying cancer cells while minimizing damage to healthy tissue. The concept of fractionation is supported by both experimental & clinical evidence. In preclinical studies, fractionation has been shown to improve the therapeutic ratio, which is the ratio of tumor cell kill to normal tissue damage, for a variety of tumor types. In clinical practice, fractionation has been used to treat many types of cancer, including breast cancer, lung cancer, & head and neck cancers (Lai *et al.,* 2019).

Fractionation schedules are based on factors such as the tumor type, size, location, & overall health of the patient. The total radiation dose & number of fractions are carefully planned and delivered to ensure optimal therapeutic benefit with minimal side effects. Overall, fractionation is a valuable tool in radiation therapy that can increase the effectiveness of cancer treatment and improve patient outcomes (Lang *et al.,* 2021)

Image-guided radiation therapy (IGRT) using imaging techniques, such as CT or MRI, to precisely target the radiation to the tumor while minimizing exposure to healthy tissue

Image-guided radiation therapy (IGRT) is a technique that uses imaging technologies, such as CT or MRI, to precisely target the radiation to the tumor while minimizing exposure to healthy tissue. IGRT involves taking images of the tumor and its surrounding tissues just prior to the delivery of each radiation treatment. This allows the radiation oncologist to accurately adjust position and shape of radiation beams to match the location & shape of the tumor, while minimizing radiation exposure to nearby healthy tissues. IGRT has several advantages over traditional radiation therapy techniques. By using imaging to guide radiation delivery, IGRT can improve the accuracy of radiation treatment and reduce the likelihood of missing the target. Additionally, IGRT can reduce the amount of radiation exposure to nearby healthy tissues, which can reduce side effects and complications from treatment. IGRT can be used for many types of cancer and has been shown to be particularly effective for tumors that are close to vital organs or sensitive structures, such as the brain or spinal cord.

The use of IGRT has become more common in recent years, as advances in imaging technology have made it easier to obtain detailed images of the tumor and surrounding tissues (Li *et al.,* 2018; Ling *et al.,* 2000). Overall, IGRT is a valuable tool in radiation therapy that allows for more precise and effective treatment while minimizing damage to healthy tissues.

Radio sensitizers using drugs that make cancer cells more susceptible to radiation, such as cetuximab, to increase the effectiveness of the radiation therapy

Radiosensitizers are drugs that make cancer cells more sensitive or susceptible to the effects of radiation

therapy. These drugs can enhance the effects of radiation therapy by promoting increased tumor cell death while sparing normal tissues. By doing so, the total radiation dose required to achieve the desired therapeutic effect can be reduced, and the likelihood of radiation-related side effects can be minimized. One example of a radiosensitizer is cetuximab, a monoclonal antibody that targets the epidermal growth factor receptor (EGFR) on cancer cells. EGFR is overexpressed in many types of cancer, including head and neck, lung, and colorectal cancer, and plays a key role in promoting cancer cell survival and proliferation. By blocking the activation of EGFR, cetuximab can enhance the effects of radiation therapy by increasing the susceptibility of cancer cells to the damaging effects of radiation (Marín *et al.,* 2000; Mayo Clinic, 2023).

Cetuximab has been shown to be particularly effective in combination with radiation therapy in the treatment of head and neck cancer. In a clinical trial, patients with locally advanced head and neck cancer who received cetuximab in combination with radiation therapy had improved overall survival and disease-free survival compared to those who received radiation therapy alone. Other examples of radio sensitizers include chemotherapy drugs such as cisplatin and fluorouracil, as well as targeted agents like imagine & lapatinib. These drugs work by differ-rent mechanisms to enhance the effects of radiation therapy and improve treatment outcomes. In summary, radio sensitizers are drugs that can increase the effectiveness of radiation therapy by making cancer cells more susceptible to the damaging effects of radiation.

Cetuximab is one example of a radio sensitizer that has been shown to be effective in combination with radiation therapy in the treatment of head & neck cancer. The use of radio sensitizers in combination with radiation therapy can improve treatment outcomes and minimize the risk of radiation-related side effects (National Cancer Institute, 2023).

Hyper fractionation: delivering radiation therapy in more frequent smaller doses per day, this approach is less common but may be useful in certain case

Hyper fractionation is a radiation therapy technique where the total radiation dose is divided into smaller, more frequent fractions per day, typically two or more, instead of one larger dose per day. This approach is less common than conventional fractionation, where the total dose is delivered once daily, but it may be useful in certain cases. Hyperfractionation is based on the principle that dividing the total radiation dose into smaller, more frequent fractions may allow for more effective tumor cell killing while minimizing damage to normal tissues. By delivering smaller doses more frequently, tumor cells are exposed to more radiation over a shorter period, while normal tissues have time to recover between treatments. Hyperfractionation may be particularly useful in the treatment of tumors that are resistant to radiation, such as some head and neck cancers. In these cases, hyperfractionation can allow for a higher total radiation dose to be delivered, potentially increasing the chances of local tumor control and improving patient outcomes (Redmond *et al.,* 2018).

Hyperfractionation may also be beneficial in certain situations where normal tissues are particularly sensitive to radiation, such as in the treatment of pediatric tumors or tumors located near critical organs. By delivering smaller doses more frequently, the total radiation dose can be increased while minimizing the risk of radiation-related side effects (Saeedi *et al.,* 2021). While hyperfractionation has potential benefits, it is not widely used in clinical practice due to several factors, including the increased treatment time and resource requirements, potential for increased side effects, and lack of strong evidence supporting its effectiveness compared to conventional fractionation. In summary, hyperfractionation is a radiation therapy technique where the total radiation dose is divided into smaller, more frequent fractions per day. While this approach may be useful in certain cases, it is less common than conventional fractionation and requires careful consideration of patient and tumor factors.

Immunotherapy using immunotherapy in combination with radiation therapy, which can enhance the body's immune system to attack cancer cells

Immunotherapy is a type of cancer treatment that harnesses the power of the immune system to attack cancer cells. By stimulating the immune system to

recognize and attack cancer cells, immunotherapy has the potential to be a highly effective treatment for a variety of cancer types. When used in combination with radiation therapy, immunotherapy has been shown to enhance the body's immune response to cancer cells, leading to improved cancer control and better patient outcomes. This is because radiation therapy can cause cancer cells to release antigens, or proteins that are recognized as foreign by the immune system, which can then be targeted by immunotherapy (Schoenhals *et al.,* 2019; Wang *et al.,* 2021). In addition, radiation therapy can also help to overcome some of the mechanisms that cancer cells use to evade the immune system, such as downregulation of major histocompatibility complex (MHC) proteins. By increasing the expression of MHC proteins, radiation therapy can help to improve the recognition & elimination of cancer cells by the immune system. Several types of immunotherapy have been used in combination with radiation therapy, including immune checkpoint inhibitors, which block the signals that cancer cells use to suppress the immune system, and adoptive cell transfer, which involves transferring immune cells that have been genetically modified to target cancer cells (Zitvogel *et al.,* 2008). While immunotherapy in combination with radiation therapy has shown promise in preclinical studies and clinical trials, it is important to note that not all patients will respond to this approach, and there may be significant side effects associated with these treatments. Careful patient selection and monitoring is essential to ensure the safety and efficacy of this approach. In summary, immunotherapy is a type of cancer treatment that enhances the body's immune system to attack cancer cells, and when used in combination with radiation therapy, can lead to improved cancer control and better patient outcomes. This approach has the potential to be a highly effective treatment for a variety of cancer types, but careful patient selection and monitoring is essential to ensure safety and efficacy.

CONCLUSION:

Radiation therapy is an important and effective treatment for cancer. However, the success of radiation therapy depends on various factors such as the type and stage of cancer, the patient's health status, and the treatment plan. To increase the effectiveness of radiation therapy, there are several approaches that can be used. Fractionation is a common method where the total radiation dose is divided into smaller, more frequent doses to reduce the risk of healthy cell damage and increase the chance of cancer cell death. Image-guided radiation therapy (IGRT) utilizes advanced imaging techniques to precisely target cancer cells while minimizing exposure to healthy tissue. Radio sensitizers are drugs that can make cancer cells more vulnerable to radiation, increasing the effectiveness of the treatment. Hyper fractionation, another approach that delivers more frequent, smaller radiation doses per day, may be useful in certain cases. Finally, immunotherapy in combination with radiation therapy is an exciting and promising method to enhance the body's immune system to attack cancer cells. The success of radiation therapy can also be improved by combining these different methods to achieve optimal results. It is important to note that the choice of the most effective approach to increasing the effectiveness of radiation therapy should be made on an individual basis, taking into account the type and stage of cancer, the patient's overall health, and other factors.

Therefore, consulting with a healthcare professional is essential to determine the most appropriate approach for each patient. In conclusion, increasing the effectiveness of radiation therapy in destroying cancer cells is a complex process that requires a multidisciplinary approach. Through a combination of advanced techniques and medical expertise, cancer patients can receive the most effective treatment plan to achieve the best possible outcomes.

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CONFLICTS OF INTEREST:

The author confirms that have no conflict of interest.

REFERENCES:

1) Alhaddad JA., and Alessa M. (2022). Barriers toward colorectal cancer screening among public in Saudi Arabia. *Eur. J. Med. Health Sci*., **4**(2), 55-63. https://doi.org/10.34104/ejmhs.022.055063

2) Bernier, J. EJ Hall A. Giaccia., (2004). *Radiation oncology: a century of achievements. Nat. Rev. Cancer*, **4**, 737-747.
3) Bernier, J., Forastiere, A., & Lefèbvre, J. L. (2005). Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemo therapy trials of the EORTC (# 22931) and RTOG (# 9501). *Head & Neck: J. for the Sciences and Specialties of the Head and Neck*, **27**(10), 843-850.
4) Boda-Heggemann J, Lohr F, Wenz F., (2011). Image-guided radiotherapy for prostate cancer. *Front Radiat Ther Oncol*, **43**, 335-346.
5) Bonner, J. A., Cohen, R. B. & Ang, K. K. (2006). Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *New England J. of Medicine*, **354**(6), 567-578.
6) Chappell, G., Pogribny, I. P., & Rusyn, I. (2016). Characterization of copy number alterations in a mouse model of fibrosis-associated hepatocellular carcinoma reveals concordance with human disease. *Cancer Medicine*, **5**(3), 574-585.
7) Chukwuma EF, Nelson OE, and Borobuebi OJ. (2022). Evaluation of serum hormones and biochemical tumor markers among breast cancer patients in the south-south region, Nigeria, *Eur. J. Med. Health Sci*., 4(6), 191-200. https://doi.org/10.34104/ejmhs.022.01910200
8) Collet, G., Szade, K., Szczepanek, K. & Kieda, C. (2016). Endothelial precursor cell-based therapy to target the pathologic angiogenesis and compensate tumor hypoxia. *Cancer letters*, **370**(2), 345-357.
9) Deorukhkar, *et al.* (2012). "Radiation-induced normal tissue injury: role of adhesion molecules in leukocyte-endothelial cell interactions." *Frontiers in Oncology*, **2**(206), https://doi.org/10.3389/fonc.2012.00206
10) Fowler, J. F. (1989). The linear-quadratic formula and progress in fractionated radiotherapy. *The British journal of radiology*, **62**(740), 679-694.
11) Hess, Jon D., and John H. Healey. (2019). "Radiation Therapy for Bone Cancer." *OrthoInfo, American Academy of Orthopaedic Surgeons*, 1. www.http//orthoinfo.aaos.org/en/treatment/radiation-therapy-for-bone-cancer/
12) Hu M, *et al.* (2021). Immunotherapy and radiotherapy: raising the bar for cancer treatment. *Cancer Lett*, **508**, 64-74
13) Jaffray, D. A. (2012). Image-guided radiotherapy: from current concept to future perspectives. *Nature reviews Clinical oncology*, **9**(12), 688-699.
14) Joiner, M. C., & Bentzen, S. M. (2018). Fractionation: the linear-quadratic approach. In *Basic clinical radiobiology* (pp. 99-111). *CRC press*.
15) Kang, J., & Pervaiz, S. (2013). Crosstalk between Bcl-2 family and Ras family small GTPases: potential cell fate regulation? *Frontiers in Oncology*, **2**, 206.
16) Kim J, Lee R, Kim J, Cho J, Yoon M. (2019.) Fractionated radiation therapy and the immune system: a primer for the radiation oncologist. *Cancer Immunol Immunother*, **68**(5), 829-842.
17) Lai X, *et al.* (2019). Comprehensive analysis of the impact of radiation-induced lymphopenia on patients with solid tumors treated with immune checkpoint inhibitors. *Cancer Immunol Immunother*, **68**(9), 1405-1415. https://doi.org/10.1007/s00262-019-02362-8
18) Lang J, *et al.* (2021). Radiotherapy & immunetherapy in cancer treatment. *Int J. Radiat Oncol Biol Phys*, **110**(1), 27-38.
19) Li, Xiang, *et al.* (2018). "Image-guided radiation therapy. https://doi.org/10.2147/ott.s185890
20) Ling, C. C., Leibel, S., & Koutcher, J. A. (2000). Towards multidimensional radiotherapy (MD-CRT): biological imaging and biological conformality. *Inter J. of Radiation Oncology* Biology* Physics*, **47**(3), 551-560
21) Marín A, *et al.* (2018). Study of the effect of radiation therapy on the nitric oxide synthase/ nitric oxide system in bladder cancer cells. *Nitric Oxide*, **79**, 1-10. https://doi.org/10.1016/j.niox,06.005
22) Mayo Clinic. Radiation therapy, (2023). Available at: https://www.mayoclinic.org/tests-procedures/radiation-therapy/about/pac-20385121
23) National Cancer Institute, (2023). Radiation Therapy and You: Support for People with Cancer.

24) "Radiation Therapy, (2020). Uses, Side Effects, and Benefits." Healthline, Healthline Media, 17. www.http//healthline.com/health/cancer/radiation-therapy

25) Redmond, *et al.* (2018). "Combined Radiotherapy and Immune Checkpoint Therapy: The Evolution of Cancer Treatment." *J. of Clinical Oncology*, **36**(22), pp. 2251-2259. https://doi.org/10.1200/jco.2017.76.5675

26) Saeedi M *et al.* (2021). Efficacy of accelerated hyperfractionated radiotherapy in advanced head and neck squamous cell carcinoma. *Int J Radiat Res*, **19**(2), 271-278.

27) Schoenhals JE, *et al.* (2021) Preclinical rationale and clinical considerations for radiotherapy plus immunotherapy: going beyond local control. *Cancer J*, **27**(1), 54-65. https://pubmed.ncbi.nlm.nih.gov/27111909/

28) Siva S, *et al.* (2019) Advances in image-guided radiation therapy. Semin Nucl Med, 49(4), 302-313.

29) Wang K, *et al.* (2021). A prospective study of accelerated hypofractionated intensity-modulated radiation therapy with simultaneous modulated accelerated radiation therapy boost for nasopharyngeal carcinoma. *Radiat Oncol*, **16**(1), 57.

30) Withers, H. R. (1985). Biologic basis for altered fractionation schemes. *Cancer*, **55**(S9), 2086-2095.

31) Zhang M. *et al.* (2016). Radiosensitization of cetuximab on esophageal squamous cell carcinoma by enhancing radiation-induced apoptosis & inhibiting radiation-induced senescence. *Oncotarget*, **7**(24), 35845-35856.

32) Zitvogel, L., Ghiringhelli, F., & Kroemer, G. (2008). Immunological aspects of cancer chemotherapy. *Nature reviews immunology*, **8**(1), 59-73.

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