Role of Nanotechnology in Cancer Radiotherapy

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Abstract

An essential component of cancer treatment has been radiotherapy. The advancement of the area was fueled by discoveries in physics, engineering, and biology. The continuing incorporation of innovations from other sectors will be essential to the development of radiation oncology. Nanomedicine is a recent branch of research that has the potential to influence radiation oncology. Materials with unique features at the nanoscale, such as superparamagnetism, increased permeability and retention effect, are ideally suited for use in radiation oncology. We will give a thorough overview of how nanotechnology might benefit cancer radiation in terms of delivery, monitoring, and diagnosis in this paper.

Keywords: Nanotechnology, Cancer, Radiotherapy

1. Introduction

One of the most popular and efficient cancer treatment options is radiotherapy. The science had its start when Nobel laureate Marie Curie learned how radiation affected human cells. Because it may produce varied DNA damage and cause cellular death in target areas (clinical and/or subclinical lesions), ionising radiation is used as a therapeutic strategy. Cancer cells divide uncontrollably, which makes them more vulnerable to radiation-induced DNA damage. Today, more than 60% of cancer patients undergo radiation as part of their anti-cancer treatment. This is done using a variety of methods, including brachytherapy and external beam (photons, protons, and electrons). The clinical indications determine the manner of application.

The therapeutic ratio of radiation has greatly increased thanks to new technologies that enable real-time imaging and better dosage distribution. However, difficulties persist. Radiation treatment is not very effective for many tumours, including glioblastoma and pancreatic cancer. In these less radioresponsive tumours, there is a need to further enhance the therapeutic efficacy of radiation. Normal tissue toxicity presents another difficulty. Chemoradiotherapy, which involves giving chemotherapy and radiation at the same time, is a common curative treatment for cancer. The combo therapy, however, also markedly raises toxicity. For instance, chemoradiotherapy for lung cancer can increase the chance of death by 5% or more, compared to either chemotherapy or radiation alone. Therefore, there is also a lot of interest in cutting down on radiotherapy's side effects [1].

Use of nanotechnology is one possible strategy to tackle these problems. The idea was inspired by the distinctive chemical and physical characteristics of nanomaterials, which set them apart from bulky or molecular materials. For instance, gold nanoparticles exhibit surface plasmon resonance and photothermal effects, whereas gold nanoclusters exhibit visible fluorescence. Nanomaterials can also be modified for high stability, biocompatibility, and interaction with specific cells because to their vast surface area. They provide a solution to several long-standing problems, particularly in the biomedical field, such medication delivery in a physiological setting or diagnostic imaging. The advantage of utilising therapeutic agents that are nanosized in oncology is that they have a longer blood circulation time, which increases their ability to effectively reach the target area.

More precisely, large carriers take use of the biological characteristics of tumours, such as damaged blood arteries with high permeability, to restrict the penetrating capacity to normal tissue and enable passive targeting of the malignant tissue. The nanocarriers can readily penetrate the damaged lymphatics within the tumour and the disrupted vasculature of the tumour. The unique properties of the nanosized therapeutic agent allow aggregation and retention of these agents within the tumour for an extended period of time once they have entered the cancer cell. The increased permeability and retention (EPR) effect is the name given to this clustering of nanocarriers inside the tumour [2].

2. Use of Nanotechnology in Cancer Radiotherapy

2.1 Improving Radioisotope Transfer Using Nanomedicine

It is commonly known that radioisotopes (radionuclides) are used in therapeutic settings. To cause single strand cleavages in DNA, radioisotopes release energy from their nucleus and produce ionised atoms and free radicals. The aberrant vasculatures in tumours may also aid in extending the retention duration of radiotherapeutics through the enhanced permeability and retention effect in addition to the augmentation of circulatory half-life by the nanoparticles. The dysfunctional tumour vasculatures are characterised by a fast proliferation of endothelial cells and a reduction in the amount of pericytes, which leads to aberrant branching components and leaky arterial walls. Macromolecules, such as nanoparticles, can readily enter the tumour through the circulatory system due to these aberrant arteries. The macromolecules that effectively perforate the tumour will be preserved inside the tumour with increased retention duration because the rapid proliferation of tumour cells disrupts lymphatic arteries and renders them ineffective in draining. Nanoparticles that have been radioisotope-labeled have been created to lessen undesirable biodistribution and boost tumour accumulation. Li et al. used copper sulphide nanoparticles labelled with the beta-emitter ^{64}Cu to prevent breast cancer. 24 hours after the intratumoral injection, more than 90% of the nanoparticles were confined to the tumour. When paired with photodynamic treatment, this radioisotope-labeled nanoparticle helped extend the life period of 4T1 bearing mice to 7.6 times longer than the control group while also reducing lung metastasis. It also exhibited no overt negative effects [3].

2.2 Improving Radiosensitizer Transfer Using Nanomedicine

Known radiosensitizers can be delivered to tumour areas more effectively when they are formulated as nanoparticles. Preclinical outcomes have demonstrated its potency as a radiosensitizer. However, due to its poor solubility, poor stability, and high toxicity, its therapeutic applicability is constrained. These issues were resolved by creating wortmannin with nanoparticles, which has a PLGA polymer core and a DSPE-PEG lipid shell. The same method was used to DNA double-strand repair inhibitors such histone deacetylase inhibitor, a potent radiosensitizer for a number of solid malignancies like colorectal cancer and prostate cancer. Through the extension of H2AX foci, the inhibitor improves the tumour cell sensitivity to radiation. However, it is very toxic and ineffective in sustaining suppression of DNA repair. The inhibitors were delivered in a controlled manner by nanoparticle encapsulation for a long-lasting impact. Some nanomaterials with high atomic numbers (Z) also have the potential to become radiosensitizers since the dosage absorbed by any tissue is linked to the Z^2 of the material, in addition to the usage of drug-loaded polymeric nanoparticles as radiosensitizers. For radiosensitizers, gold nanoparticles (Z=79) are the most often utilised high Z nanomaterials. Ultrasmall $Au_{29-43}(SG)_{27-37}$ nanoclusters with glutathione coating have been used as radiosensitizers, according to Xie et al. At 24 hours after injection, the

nanosensitizers demonstrated a significant tumour absorption of around 8.1% ID/g. The administration of gold nanoclusters dramatically enhanced the tumor's resistance to radiation [4].

2.3 Decrease in Side Effects due to Nanomedicine

The distribution of radiosensitizers or radioisotopes in healthy tissues can be reduced, and the release of these radiotherapeutic substances can be controlled, to lessen adverse effects. Radiation therapy's adverse effects are frequently brought on by unanticipated harm to healthy tissue. The tumoricidal action of radiation can be enhanced and synergistically improved by the use of radiosensitizers. Therefore, the use of radiosensitizers will enable lower radiation doses to achieve the same or greater tumor-killing efficacy. However, radiosensitizers' generalised biodistribution will cause toxicity in healthy organs. The same is true for radioisotopes, whose buildup in healthy tissues will result in immediate harm. It has been demonstrated that normal capillaries and vasculature in a variety of bodily areas, including the skin, lungs, and heart, are less permeable to nanoparticles. As a result, longer exposure to the agents caused by the regulated and continuous release of nanoparticles into the tissue has been linked to improved effects and higher tolerance for normal tissues. The therapeutic application of Doxil, which significantly decreased the cardiotoxicity of doxorubicin without reducing its anti-tumor activity, served as a demonstration of this. Furthermore, the release is conditional due to chemical interaction between radiotherapeutic drugs and nanoparticles. It can either react to factors present in the tumour microenvironment, such as low pH, redox, or enzymes, or it can react to outside stimuli, such as a change in temperature or a magnetic field. Such methods significantly reduce the drugs' release in blood vessels or healthy tissues, potentially decreasing the negative effects [5].

3. Chemoradiotherapy

Chemoradiotherapy can be made easier by nanotechnology in two ways. Due to several chemotherapy medications, such as cisplatin, doxorubicin, and paclitaxel, having a radiosensitizing effect, one approach is to administer chemotherapeutics via nanoparticles paired with external irradiation for combination treatment. The second method provides simultaneous delivery of drugs to the lesion as well as precise ratio control by combining the administration of chemotherapeutics and radiosensitizers/radioisotopes in one nanoparticle. Due to the reasons previously described, both nanotechnology methods gain from lower toxicity in healthy tissues and preferential accumulation in tumours [6].

4. Challenges in Nanotechnology based Radiotherapy

For many years now, nanomedicine has been seen as a potential topic for solving many medical issues. A few medications, like as Doxil or Abraxane, have been commercialised for the treatment of clinical cancer. Instead, because the efficacy is not as strong as it suggests in animal models, the majority of attempts at nanoparticle-based human trials failed. More and more clinical data are putting the enhanced permeability and retention effect, one of the field's most significant pillars, under scrutiny. With a better understanding of the tumour microenvironment, it appears that the little improvement in treatments brought about by the EPR effect is insufficient to effectively treat cancer. The lengthy nanoparticle circulation period may also enhance systemic toxicity [7].

5. Conclusions

The delivery and/or concentration of radiosensitizers or radioisotopes can be potentiated using nanotechnology to increase their anti-tumor efficacy. Recent research on the impact of radiation on tumour microenvironments has also sparked interest in alternative radiotherapy combination therapies, particularly those that combine radiotherapy with immunotherapy. Radiation therapy increases the exposure to and presentation of tumour antigens, which prompts the signalling of inflammatory cytokines and the recruitment of immune cells. Although cancer immunotherapy techniques like checkpoint inhibition and chimeric antigen receptor (CAR) T cell treatment have shown encouraging clinical outcomes, their combination with nanotechnology is still being researched. Adaptive radiotherapy, commonly known as IGRT, can be performed using nanotechnology in imaging. Therefore, in our opinion, it is crucial to keep researching how nanotechnology can enhance radiotherapy's capacity to harm cancer cells. The constraint of dosage escalation (radiosensitizers, radioisotopes), as well as physical-technical aspects (IGRT) that can be modified to further increase therapeutic efficacy, may be overcome using nanotechnology.

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